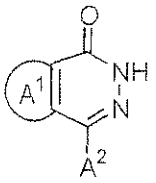
There is therefore a need in the therapeutic arts for PARP inhibitors. Such compounds can be used to treat subjects suffering from cancer, and can further expand the range of treatment options available for such subjects.

SUMMARY ~~OF THE INVENTION~~

One embodiment of this ~~invention~~disclosure, therefore, pertains to compounds that inhibit the activity of poly(ADP-ribose) polymerase and have formula I



(I),

and pharmaceutically acceptable salts thereof, wherein

A^1 is R^1 or R^2, wherein A^1 is unsubstituted or substituted with one or two OH, CN, C_1-alkyl, C_2-alkyl, C_3-alkyl, C_4-alkyl, C_5-alkyl, cycloalkane, OR^A or NR^AR^A;

R^A is H or alkyl;

R^1 is cycloalkane or cycloalkene each of which is unfused or fused with R^{1A};

R^{1A} is benzene, heteroarene, cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

R^2 is heterocycloalkane or heterocycloalkene; each of which is unfused or fused with R^{2A};

R^{2A} is benzene, heteroarene, cycloalkane, cycloalkene, heterocycloalkane or heterocycloalkene;

A^2 is OR^4, NHR^4, $N(R^4)_2$, SR^4, $S(O)R^4$, SO_2R^4 or R^5;

wherein each R^4 is C_1-alkyl, C_2-alkyl or C_3-alkyl; each of which is substituted with R^{10};

N-cyclopropyl-2-fluoro-5-((5-oxo-1,2,3,4,5,6-hexahydropyrido(2,3-d)pyridazin-8-yl)methyl)benzamide;

8-(3-((4-(2-ethoxyethyl)piperazin-1-yl)carbonyl)-4-fluorobenzyl)-2,3,4,6-tetrahydropyrido(2,3-d)pyridazin-5(1H)-one;

2-fluoro-5-((5-oxo-1,2,3,4,5,6-hexahydropyrido(2,3-d)pyridazin-8-yl)methyl)-N-(2-piperidin-1-ylethyl)benzamide;

2-fluoro-5-((5-oxo-1,2,3,4,5,6-hexahydropyrido(3,2-d)pyridazin-8-yl)methyl)-N-(2-oxo-2-(piperidin-1-yl)ethyl)benzamide;

4-(4-fluoro-3-((4-pyrimidin-2-ylpiperazin-1-yl)carbonyl)benzyl)-5,6,7,8-tetrahydrophthalazin-1(2H)-one; and

4-(4-fluoro-3-(2-oxopyrrolidin-1-yl)phenyl)-5,6,7,8-tetrahydrophthalazin-1(2H)-one;

and therapeutically salts, prodrugs, esters, amides, salts of prodrugs, salts of esters and salts of amides thereof.

In one aspect, there is provided a compound 1-(2-fluoro-5-((4-oxo-3,4,5,6,7,8-hexahydrophthalazin-1-yl)methyl)phenyl)pyrrolidine-2,5-dione, or a pharmaceutically acceptable salt thereof.

In one aspect, there is provided a pharmaceutical composition comprising a compound as defined herein and a pharmaceutically acceptable excipient.

In one aspect, there is provided a compound as defined herein for use in treating cancer in a mammal by administering thereto a therapeutically acceptable amount of said compound.

DETAILED DESCRIPTION OF THE INVENTION

Variable moieties of compounds herein are represented by identifiers (capital letters with numerical and/or alphabetical superscripts) and may be specifically embodied.

It is meant to be understood that proper valences are maintained for all combinations herein, that monovalent moieties having more than one atom are attached through their left ends.

It is also meant to be understood that a specific embodiment of a variable moiety may be the same or different as another specific embodiment having the same identifier.

Abbreviations which have been used in the descriptions of the schemes and the examples that follow are:

BOC is Di-*tert*-butyl dicarbonate

C-18 is dimethyl-octadecylsilane

DCI for chemical ionization for direct introduction,

DME for 1,2-dimethoxyethane,

DMSO for dimethylsulfoxide,

ESI for electrospray ionization,

HATU for O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate,