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(54) **AMIDE SUBSTITUTED INDAZOLES AS POLY(ADP-RIBOSE)POLYMERASE(PARP) INHIBITORS**

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(58) **Field of Classification Search** 514/322; 546/199

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

6,100,283	A	8/2000	Griffin et al.
6,310,082	B1	10/2001	Griffin et al.
6,448,271	B1	9/2002	Lubisch
6,509,365	B1	1/2003	Lubisch
6,696,437	B1	2/2004	Lubisch
6,737,421	B1	5/2004	Lubisch
7,041,675	B2	5/2006	Lubisch
7,087,637	B2	8/2006	Grandel
2006/0063926	A1	3/2006	Ma et al.
2006/0229289	A1	10/2006	Zhu et al.
2006/0229351	A1	10/2006	Zhu et al.
2007/0112047	A1	5/2007	Penning et al.
2007/0259937	A1	11/2007	Giranda et al.
2009/0062268	A1*	3/2009	Chu 514/230.5
2009/0197863	A1*	8/2009	Chu et al. 514/210.21
2009/0275619	A1	11/2009	Boueres et al.

FOREIGN PATENT DOCUMENTS

CA	2349227	2/2008
EP	0 879 820	12/2001
WO	WO97/04771	2/1997
WO	WO 99/59973	11/1999
WO	200026193 A1	5/2000
WO	WO00/26192	5/2000
WO	WO00/29384	5/2000
WO	WO00/32579	6/2000
WO	WO00/64878	11/2000
WO	WO00/68206	11/2000
WO	WO 01/21615	3/2001
WO	WO01/57038	8/2001
WO	WO01/85687	11/2001
WO	WO 02/068407	9/2002
WO	WO03/007959	1/2003
WO	WO 03/062234	7/2003
WO	WO 03/106430	12/2003
WO	WO 2004/014861	2/2004
WO	WO2005/066136	7/2005
WO	WO2007/041357	4/2007
WO	2007113596 A1	10/2007

OTHER PUBLICATIONS

Grever et al. "National cancer inst . . . " Seminar in Oncology 19(6) 622-638 (1992).*

Cancer Classification p. 1-3 (2005) internet.*

Bouerer et al. "Preparation of amide . . . " CA 148:448784 (2007).*

Huw D. Thomas, et al., Molecular Cancer Research, vol. 6 (3), pp. 945-956 (2007).

Office Action mailed Oct. 10, 2010 for U.S. Appl. No. 12/225,857, (2010).

Boueres, J. et al., Preparation of amide substituted indazole and benzotriazole derivatives as poly(ADP-ribose) polymerase (part) inhibitors, Caplus 147:448784 (2007).

Categories of Cancer/ Cancer Classification, pp. 1-3; http://training.seer.cancer.gov/modules_...ase/unit3_categories2_by_histology.html, (2005).

Grever, M. et al., "The National Cancer Institute: Cancer Drug Discovery and Development Program", Seminars in Oncology, 19(6):622-638 (Dec. 1992).

(Continued)

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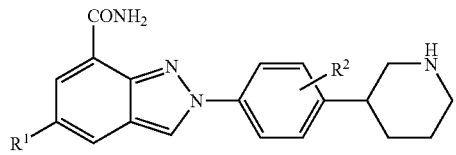
(57) **ABSTRACT**

The present invention relates to compounds of formula I:

(I)



and pharmaceutically acceptable salts, stereoisomers or tautomers thereof which are inhibitors of poly (ADP-ribose) polymerase (PARP) and thus useful for the treatment of cancer, inflammatory diseases, reperfusion injuries, ischemic conditions, stroke, renal failure, cardiovascular diseases, vascular diseases other than cardiovascular diseases, diabetes, neurodegenerative diseases, retroviral infection, retinal damage or skin senescence and UV-induced skin damage, and as chemo- and/or radiosensitizers for cancer treatment.

9 Claims, No Drawings