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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS OF TREATING OR PREVENTING CANCER USING PYRIDINE CARBOXALDEHYDE PYRIDINE THIOSEMICARBAZONE RADIOSENSITIZING AGENTS

(57) Abstract: The present invention features methods of inhibiting ribonucleotide reductase and DNA synthesis after administration of a dose of ionizing radiation to cells. The present invention further features methods of treating patients suffering from cancer comprising contemporaneous or sequential administration of a radiosensitizing dose of a 2-carboxyaldehyde pyridine thiosemicarbazone compound and ionizing radiation.



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INTERNATIONAL SEARCH REPORT

International application No

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A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K31/44 C07D213/02 A61P35/00

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)

A61K C07D

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 practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data, BEILSTEIN Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	<p>BARKER CHRISTOPHER A ET AL: "In vitro and in vivo radiosensitization induced by the ribonucleotide reductase inhibitor Triapine (3-aminopyridine-2-carboxaldehyde-thiosemicarbazone)."</p> <p>CLINICAL CANCER RESEARCH : AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH 1 MAY 2006, vol. 12, no. 9, 1 May 2006 (2006-05-01), pages 2912-2918, XP002415581</p> <p>ISSN: 1078-0432</p> <p>the whole document</p> <p style="text-align: center;">----- -/--</p>	1-67

☒ 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 document 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
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- *&* document member of the same patent family

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/036044

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	<p>BARKER ET AL: "3-Aminopyridine-2-Carboxaldehyde Thiosemicarbazone (Triapine): A Ribonucleotide Reductase Inhibitor with Potent Radiosensitizing Properties" INTERNATIONAL JOURNAL OF RADIATION: ONCOLOGY BIOLOGY PHYSICS, PERGAMON PRESS, US, vol. 63, 1 October 2005 (2005-10-01), page S170, XP005083302 ISSN: 0360-3016 the whole document</p>	1-67
Y,P	<p>WO 2006/078903 A1 (MATTHEWS RICHARD H [US]) 27 July 2006 (2006-07-27) claim 5</p>	1-67
Y	<p>SHEWACH D S ET AL: "Gemcitabine and radiosensitization in human tumor cells." INVESTIGATIONAL NEW DRUGS 1996, vol. 14, no. 3, 1996, pages 257-263, XP009077486 ISSN: 0167-6997 page 258</p>	1-67
Y	<p>GREGOIRE VINCENT ET AL: "Chemo-radiotherapy: Radiosensitizing nucleoside analogues (Review)" ONCOLOGY REPORTS, vol. 6, no. 5, September 1999 (1999-09), pages 949-957, XP009077509 ISSN: 1021-335X page 950 - page 951 page 952</p>	1-67
Y	<p>WO 2004/082579 A2 (PHARMACIA ITALIA SPA [IT]; GERONI MARIA CRISTINA ROSA [IT]; PACCIARINI) 30 September 2004 (2004-09-30) claim 14</p>	1-67
Y	<p>WO 01/91794 A2 (UNIV VIRGINIA COMMONWEALTH [US]; GEWIRTZ DAVID A [US]) 6 December 2001 (2001-12-06) claims 26-43</p>	1-67
Y	<p>MOORE E C ET AL: "Inhibition of ribonucleotide reductase by [alpha]-(N)-heterocyclic carboxaldehyde thiosemicarbazones" PHARMACOLOGY AND THERAPEUTICS 1984 UNITED KINGDOM, vol. 24, no. 3, 1984, pages 439-447, XP002417442 page 441 page 445</p>	1-67

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/036044

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	"Triapine, a ribonucleotide reductase inhibitor, enhances incorporation of gemcitabine into DNA and cytotoxicity to KB cells" EUROPEAN JOURNAL OF CANCER, PERGAMON PRESS, OXFORD, GB, vol. 38, November 2002 (2002-11), page S26, XP004403510 ISSN: 0959-8049 the whole document	1-8, 10-31, 33-67
Y	LI J ET AL: "Synthesis and biological evaluation of a water soluble phosphate prodrug of 3-aminopyridine-2-carboxaldehyde thiosemicarbazone (3-AP)" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 8, no. 22, 17 November 1998 (1998-11-17), pages 3159-3164, XP004143719 ISSN: 0960-894X page 3161 - page 3162	1-67
Y	US 5 767 134 A (LI JUN [US] ET AL) 16 June 1998 (1998-06-16) cited in the application column 1; claim 13	1-4, 9-27, 32-70
Y	EP 0 570 294 A1 (UNIV YALE [US]) 18 November 1993 (1993-11-18) claim 1	1-8, 10-31, 33-70
Y	KLAYMANN ET AL: "2-acetylpyridine thiosemicarbazones" ARZNEIM-FORSCH/DRUG RES, vol. 33(II), no. 7, 1987, pages 909-912, XP001071299 ISSN: 0162-0134 page 911; table 8	68-70
Y,P	WO 2005/087211 A (UNIV CALIFORNIA [US]; UNIV CAPE TOWN [ZA]; CHIBALE KELLY [ZA]; GREENBA) 22 September 2005 (2005-09-22) claim 1	68-70
Y	CHUNG THEODORE D ET AL: "Molecular targeting in radiotherapy: epidermal growth factor receptor." MOLECULAR INTERVENTIONS FEB 2005, vol. 5, no. 1, February 2005 (2005-02), pages 15-19, XP002415585 ISSN: 1534-0384 page 15 - page 16	1-67
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/036044

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BAUMANN M ET AL: "Molecular targeting in radiotherapy of lung cancer" LUNG CANCER, ELSEVIER, AMSTERDAM, NL, vol. 45, August 2004 (2004-08), pages S187-S197, XP004640965 ISSN: 0169-5002 page S188 - page S189 -----	1-67

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Box 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:

Although claims 1-2 and 4-67 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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 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:

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 fee, this Authority did not invite payment of any additional fee.
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.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/036044

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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