(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
23 February 2006 (23.02.2006)

PCT

(10) International Publication Number
WO 2006/020403 A3

(51) International Patent Classification:
A61K 31/22 (2006.01) *A61P 35/02* (2006.01)
A61K 47/06 (2006.01) *A61P 43/00* (2006.01)
A61P 35/00 (2006.01)

(21) International Application Number:
PCT/US2005/026702

(22) International Filing Date: 28 July 2005 (28.07.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/591,643 28 July 2004 (28.07.2004) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
1 June 2006

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.

WO 2006/020403 A3

(54) Title: 3-HALO-2-OXOPROPIONATE SALTS AND ESTERS AS NOVEL ANTICANCER AGENTS

(57) Abstract: The present invention is directed to compositions that inhibit glycolysis, preferentially in cancer. Specifically, the anticancer compositions comprise 3-halo-2-oxopropionate and its derivatives, such as ester derivatives. However, in specific embodiments, the anticancer composition is sodium 3-halo-2-oxopropionate, such as sodium 3-bromo-2-oxopropionate and a stabilizing agent, such as carbonic acid. In particular embodiments, the compositions of the present invention further comprise a metabolic intermediate for normal cells to utilize in a pathway for an alternate energy source, thereby providing protection to normal cells. In other embodiments, the 3-halo-2-oxopropionate or its ester derivative is used in combination with an additional cancer therapy, such as radiation and/or a drug.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
A61K31/22 A61K47/06 A61P35/00 A61P35/02 A61P43/00

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

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, PAJ, CHEM ABS Data, MEDLINE, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/087961 A1 (KO YOUNG HEE ET AL) 8 May 2003 (2003-05-08) cited in the application abstract paragraph '0007! - paragraph '0011! paragraph '0064! - paragraph '0069! paragraph '0070! paragraph '0092! - paragraph '0094! paragraph '0101! - paragraph '0110! paragraph '0134! - paragraph '0135! paragraph '0170! claims 1-49 ----- -/--	1-9, 11-16, 19-45

[X] Further documents are listed in the continuation of Box C.

[X] 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

Date of the actual completion of the international search	Date of mailing of the international search report
31 January 2006	28/02/2006

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Taylor, G.M.

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2003/181393 A1 (LAMPIDIS THEODORE J ET AL) 25 September 2003 (2003-09-25) cited in the application abstract paragraph '0002! paragraph '0020! - paragraph '0021! paragraph '0042! - paragraph '0044! claims 6-8	1-4,11, 19-45
X	WO 94/02108 A (THE JOHNS HOPKINS UNIVERSITY) 3 February 1994 (1994-02-03) cited in the application page 5, line 8 - page 6, line 16 tables 2,4 claims 1-34	1,2, 11-45
X	GESCHWIND J-F H ET AL: "Novel therapy for liver cancer: Direct intraarterial injection of a potent inhibitor of ATP production" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 62, 15 July 2002 (2002-07-15), pages 3909-3913, XP002969687 ISSN: 0008-5472 cited in the application abstract Materials and Methods: Intraarterial Injection of 3-BrPA page 313, last paragraph	1,2, 11-45
X	KO, Y H; PEDERSEN, P L; GESCHWIND, J F: "Glucose catabolism in the rabbit VX2 tumour model for liver cancer: characterisation and targeting hexokinase" CANCER LETT., vol. 173, 2001, pages 83-91, XP002365255 cited in the application abstract Discussion	1,2, 11-45
P,X	XU, R-H ET AL.: "Inhibition of glycolysis in cancer cells: a novel strategy to overcome drug resistance associated with mitochondrial respiratory defect and hypoxia" CANCER RES., vol. 65, no. 2, 15 January 2005 (2005-01-15), pages 613-621, XP002365256 cited in the application abstract Discussion	1-45

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2003/013487 A1 (JOO WON-IL) 16 January 2003 (2003-01-16) cited in the application abstract claims 1-32	1-45
A	TUNNICLIFF, G; NGO, T T: "Mechanism of inactivation of brain glutamic decarboxylase by 3-bromopyruvate" INT. J. BIOCHEM., vol. 9, 1978, pages 249-252, XP002365257 cited in the application the whole document	1-45

INTERNATIONAL SEARCH REPORT

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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. [X] Claims Nos.: 20-39
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 20-39 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
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