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14 August 2008



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(54) **Title:** USE OF VITAMIN D DERIVATIVES TO ENHANCE DELIVERY OF THERAPEUTICS AND OXYGEN TO TUMORS

(57) **Abstract:** Disclosed is a method of treating a hyperproliferative disease or other condition in an animal comprising administering a vitamin D compound or a mimic thereof by high dose pulse administration. Said hyperproliferative disease is characterized by diminished performance status, elevated or diminished level of inflammatory biomarker, reduced response to tumor therapeutic agent and impaired perfusion and/or hypoxia. Disclosed is a method of treating a hyperproliferative disease or other condition in an animal by first determining the performance status of the animal, detecting a biomarker of inflammation and determining whether the tumor or other tissue exhibits impaired perfusion and/or hypoxia. Administration of a vitamin D compound or mimic thereof improves the delivery of a therapeutic agent to tumors or other tissues, improves the oxygenation of tumors or other tissues, reduces inflammation of tumors or other tissues and improves the quality of palliative care of terminal cancer patients.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US 07/23030

A CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61 K 31/56 (2008 01) USPC - 514/167, 514/168' 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) USPC- 514/167, 514/168		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC-514/167, 514/168 (text search-see search terms below)		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PubWEST (USPT, PGPB, EPAB, JPAB) and Google Patent/Scholar Search terms vitamin D, tumor, biomarker, inflammation, perform status, hypoxia, perfusion, C reactive protein, end stage cancer		
C DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X ----- Y	US 6,521,608 B1 (Henner et al) 18 February 2003 (18 02 2003) abstract, col 5, ln 17-52, col 2, ln 64-67, col 12, ln 64-65	1, 2 ----- 3-9, 12, 14, 16-18, 20, 30, 32-33
X ----- Y	US 2004/0253323 A1 (Giles) 16 December 2004 (16 12 2004) abstract, para [0019], [0033], [0036], [0040], [0042], [0044], [0069]	10-11, 15, 21-22 ----- 8-9, 12-13, 14, 16-20, 30, 32-33
Y	US 5,654,333 A (Samid) 05 August 1997 (05 08 1997) abstract, col 56, ln 43-44, col 55, ln 30-55	3-7, 13-14, 16-20
Y	US 2004/0191263 A1 (Hageman et al) 30 September 2004 (30 09 2004) abstract, para [0005], [0058], [0063]	5,7, 16-18
Y	US 2006/0078494 A1 (Polvino) 13 April 2006 (13 04 2006) abstract, para [0008]	30, 33
Y	US 6,503,893 B2 (Bishop et al) 07 January 2003 (07 01 2003) abstract, col 3, ln 6	32-33
<input type="checkbox"/> Further documents are listed in the continuation of Box C <input type="checkbox"/>		
* Special categories of cited documents	"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	
"A" document defining the general state of the art which is not considered to be of particular relevance	"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	
"E" earlier application or patent but published on or after the international filing date	"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	
"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)	"&" document member of the same patent family	
"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		
Date of the actual completion of the international search 19 February 2008 (19 02 2008)	Date of mailing of the international search report 17 APR 2008	
Name and mailing address of the ISA/US Mail Stop PCT, Attn ISA/US, Commissioner for Patents P O Box 1450, Alexandria, Virginia 22313-1450 Facsimile No 571-273-3201	Authorized officer Lee W Young PCT Helpdesk 571 272-4300 PCT OSP- 571 272 7774	

Box No. 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 **I** Claims Nos
because they relate to subject matter not required to be searched by this Authority, namely
- 2 **D** 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 **LAI** Claims Nos 23-29, 31, 34
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6 4(a)

Box No. 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 **I** As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
- 2 **I** As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees
- 3 **D** 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 **I** 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 and, where applicable, the payment of a protest fee
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation
- No protest accompanied the payment of additional search fees