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(54) Title: THERAPEUTIC COMPOSITION

(57) Abstract: An anti-mitotic composition with a therapeutic index greater than 1.1 , a clonogenic survival rate of less than 0.1 percent, and a binding affinity index for a class II, a class III, or a class V beta tubulin isot e of at least about 1.1.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US06/00052

A. CLASSIFICATION OF SUBJECT MATTER
IPC: **A61K 31/12**(2006.01)

USPC: 514/675
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)
U.S. : 514/675

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 practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KELNER et al. Enhanced Antitumor Activity of Irofulven in Combination with Antimitotic Agents. Investigational New Drugs, 2002, Vol. 20, pages 271-279.	1-20
X	HAMMOND et al. Enhanced Antitumor Activity of 6-hydroxymethylacylfulvene in Combination with Topotecan or Paclitaxel in the MV522 Lung Carcinoma Xenograft Model. European Journal of Cancer, 2000, Vol. 36, pages 2430-2436.	1-20
X	SCHNEIDER et al. Resveratrol Analog (Z)-3,5,4'-Trimethoxystilbene is a Potent Anti-Mitotic Drug Inhibiting Tubulin Polymerization. Int. J. Cancer, 2003, Vol. 107, pages 189-196.	1
Y	THOMAS et al. Phase I Clinical and Pharmacokinetic Trial of Irofulven. Cancer Chemther. Pharmacol., 2001, Vol. 48, pages 467-472.	1-20

☒ 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 application or patent 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

"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

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Date of the actual completion of the international search
12 April 2007 (12.04.2007)

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INTERNATIONAL SEARCH REPORT

International application No.
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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.
Y	FITZPATRICK et al. The Immunopharmacology of Paclitaxel (Taxol) and Docetaxel (Taxotere), and Related Agents. International Immunopharmacology, 2003, Vol. 3, pages 1699-1714.	1-20
A	BRITTEN et al. Enhanced Antitumor Activity of 6-hydroxymethylacylfulvene in Combination with Irinotecan and 5-fluorouracil in the HT29 Human Colon Cancer Tumor Xenograft Model. Cancer Research, 1999, Vol. 59, pages 1049-1053.	1-20
A	US 3,997,506 (DUGAT, P.) 14 December 1976 (14.12.1976), entire document.	1-20

INTERNATIONAL SEARCH REPORT

International application No.
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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. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 1-20
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:
Please See Continuation Sheet

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 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. ☐ 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 additional fees, this Authority did not invite payment of any additional fees.
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 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.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US06/00052

Continuation of Box II Reason 2:
The claims and the disclosure supporting the claims are not searchable because it is not at all clear what applicant is claiming. The compositions recited in the claims are only defined by characteristics of the overall composition, however there is no description of exactly what agent(s) might provide a composition that: (i) is anti-mitotic; (ii) has a therapeutic index greater than 1.1; (iii) has a clonogenic survival rate of less than 0.1 percent; and (iv) has a binding affinity for a beta tubulin isotype of at least 1.1. To search the full scope of the instant claims would be impossible given the present disclosure, which quotes from and incorporates by reference hundreds of patents and publications. Further, no specific agents are described or contemplated in the disclosure.

Continuation of B. FIELDS SEARCHED Item 3:
PubMed, U.S. Patent documents

Search Terms: irofulvene, anti-mitotic, paclitaxel