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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: MICROTUBULE STABILIZING COMPOUNDS

(57) Abstract: Laulimalide and epothilone derivatives useful as microtubule stabilizing agents, and in the treatment of cancers are disclosed. Methods of making the compounds and using the compounds as therapeutic agents in treating cancers also are disclosed.



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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 03/06457

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D493/08 C07D493/18 A61K31/439 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)

IPC 7 C07D A61K A61P

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GHOSH ARUN K ET AL: "Total Synthesis of (-)-Laulimalide" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC, US, vol. 122, 2000, pages 11027-11028, XP002189882 ISSN: 0002-7863 cited in the application examples 19,20 page 11028, column 2 ----- -/--	1,9,10



Further documents are listed in the continuation of box C.



Patent family members are listed in 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

"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.

"&" document member of the same patent family

Date of the actual completion of the international search

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Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 03/06457

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GHOSH A K ET AL: "A macrolactonization-based strategy to obtain microtubule- stabilizing agent (-)-laulimalide" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 42, 2001, pages 3399-3401, XP002189881 ISSN: 0040-4039 examples 8,9,15 -----	1
X	WO 01 54689 A (UNIV HAWAII ;UNIV UTAH STATE (US); DAVIDSON BRADLEY S (US); MOOBER) 2 August 2001 (2001-08-02) claims 1,5,15 -----	1,9,10
P,X	WO 02 064589 A (KOSAN BIOSCIENCES INC) 22 August 2002 (2002-08-22) scheme 15 -----	1
E	EP 1 295 886 A (SCHERING AG) 26 March 2003 (2003-03-26) examples 7A,7B -----	1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/06457

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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 10-15 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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

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.:

1,3-19 (all partially

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

International Application No. PCT/US 03/06457

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1, 3-19 (all partially)

Compounds according to the 1st and 2nd general formulae of claim 1 as well as their pharmaceutical use and compositions.

2. claims: 1, 3-7, 9-19

Compounds according to the 3rd general formula of claim 1 as well as their pharmaceutical use and composition.

3. claims: 1, 3-6, 9-19 (all partially)

Compounds according to the 4th general formula of claim 1 as well as their pharmaceutical use and composition.

4. claims: 1, 3-7, 9-10 (all partially)

Compounds according to the 5th general formula of claim 1 as well as their pharmaceutical use and composition.

5. claims: 1, 3-7, 9-10 (all partially)

Compounds according to the 6th general formula of claim 1 as well as their pharmaceutical use and composition.

6. claims: 2-7, 9-19 (all partially)

Compounds according to the 1st and 2nd general formulae of claim 2 as well as their pharmaceutical use and composition.

7. claims: 2-7, 9-19 (all partially)

Compounds according to the 3rd general formula of claim 2 as well as their pharmaceutical use and composition.

8. claims: 2-7, 9-19 (all partially)

Compounds according to the 4th general formula of claim 2 as well as their pharmaceutical use and composition.

9. claims: 2-7, 9-19 (all partially)

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 03/06457

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Compounds according to the 5th general formula of claim 2 as well as their pharmaceutical use and composition.

10. claims: 2-7, 9-19 (all partially)

Compounds according to the 6th general formula of claim 2 as well as their pharmaceutical use and composition.

11. claims: 2-7, 9-19 (all partially)

Compounds according to the 7th general formula of claim 2 as well as their pharmaceutical use and composition.

12. claims: 2-7, 9-19 (all partially)

Compounds according to the 8th general formula of claim 2 as well as their pharmaceutical use and composition.

13. claims: 2-7, 9-19 (all partially)

Compounds according to the 9th general formula of claim 2 as well as their pharmaceutical use and composition.

14. claims: 2-7, 9-19 (all partially)

Compounds according to the 10th general formula of claim 2 as well as their pharmaceutical use and composition.

15. claims: 2-7, 9-19 (all partially)

Compounds according to the 11th general formula of claim 2 as well as their pharmaceutical use and composition.

16. claim: 7 (partially)

Compounds according to claim 7 as depicted on page 114.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 03/06457

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0154689	A	02-08-2001	US 6414015 B1 AU 3117301 A WO 0154689 A1 US 2002198256 A1	02-07-2002 07-08-2001 02-08-2001 26-12-2002
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EP 1295886	A	26-03-2003	EP 1295886 A1 WO 03024975 A1	26-03-2003 27-03-2003