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

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                          |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------|
| <b>(51) International Patent Classification <sup>5</sup> :</b><br><b>A61K 31/00, 31/725</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | <b>A3</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | <b>(11) International Publication Number:</b> <b>WO 94/05267</b><br><b>(43) International Publication Date:</b> 17 March 1994 (17.03.94) |
| <b>(21) International Application Number:</b> PCT/GB93/01848<br><b>(22) International Filing Date:</b> 1 September 1993 (01.09.93)<br><b>(30) Priority data:</b><br>9218510.7 1 September 1992 (01.09.92) GB<br><b>(71) Applicant (for all designated States except US):</b> MEDICAL RESEARCH COUNCIL [GB/GB]; 20 Park Crescent, London W1N 4AL (GB).<br><b>(72) Inventors; and</b><br><b>(75) Inventors/Applicants (for US only) :</b> HOFFMAN, Richard, Michael [GB/GB]; 273 Hinton Way, Great Shelford, Cambridge CB2 5AN (GB). PAPER, Dietrich, Herbert, Walter [DE/DE]; Ockerstrasse 12, D-93142 Maxhutte-Haidof (DE). | <b>(74) Agent:</b> KEITH W NASH & CO; Pearl Assurance House, 90-92 Regent Street, Cambridge CB2 1DP (GB).<br><b>(81) Designated States:</b> AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).<br><b>Published</b><br><i>With international search report.</i><br><i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i><br><b>(88) Date of publication of the international search report:</b><br>28 April 1994 (28.04.94) |                                                                                                                                          |
| <b>(54) Title:</b> USE OF CARRAGEENANS AS GROWTH FACTOR ANTAGONISTS<br><br><b>(57) Abstract</b><br><br>Disclosed is a substance, being a carrageenan or a derivative thereof, for use as growth factor suppressor or inhibitor. The substances disclosed as being useful as growth factor inhibitors are useful in the treatment of tumours and other conditions where growth factors are involved.                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                          |

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A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 5 A61K31/00 A61K31/725

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 5 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                            | Relevant to claim No.     |
|------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|
| X          | CELL REGUL.,<br>vol.1, no.11, 1990<br>pages 833 - 842<br>R. ISHAI-MICHAELI ET AL 'heparanase<br>activity expressed by platelets,<br>neutrophils and lymphoma cells releases<br>active fibroblast growth factor from<br>extracellular matrix.'<br>see page 834 | 1,2                       |
| X          | INT. J. CANCER,<br>vol.39, no.1, 1987<br>pages 82 - 88<br>D.R. COOMBE ET AL. 'Analysis of the<br>inhibition of tumour metastasis by<br>sulphated polysaccharides.'<br>see the whole document                                                                  | 1-5,7,<br>10,11,<br>13-16 |
|            | ---<br>-/--                                                                                                                                                                                                                                                   |                           |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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- "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

12 November 1993

Date of mailing of the international search report

29.03.94

Name and mailing address of the ISA

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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                                                    | HYDROBIOLOGIA,<br>vol.204/205, 1990<br>pages 577 - 584<br>H. NODA ET AL 'Antitumor activity of<br>marine algae.'<br>* whole document especially table 3 *                                                                                                                                                                                                                                | 1-7,10,<br>11,13-16   |
| X                                                    | J. PHARMACO-BIODYN.,<br>vol.7, no.7, 1984<br>pages 465 - 471<br>T. MATSUMOTO ET AL. 'Growth inhibition of<br>leukemia L-1210 ascites tumor by<br>combination of carrageenan and mitomycin C<br>in vivo.'<br>see the whole document                                                                                                                                                       | 1-8,10,<br>11,13-16   |
| X                                                    | CHEMICAL ABSTRACTS, vol. 95, no. 9,<br>31 August 1981, Columbus, Ohio, US;<br>abstract no. 73721g,<br>E. OHTSUKA 'Activation of cytotoxic<br>macrophages by carrageenan with special<br>reference to iota- carrageenan.'<br>see abstract<br>& NICHIDAI IGAKU ZASSHI,<br>vol.40, no.6, 1981<br>pages 521 - 528                                                                            | 1-7,10,<br>11,13-16   |
| X                                                    | CHEMICAL ABSTRACTS, vol. 89, no. 3,<br>17 July 1978, Columbus, Ohio, US;<br>abstract no. 22078w,<br>R.G.P. PUGH-HUMPHREYS ET AL 'The effect of<br>the macrophage cytotoxic agent<br>iota-carrageenan on the growth of two<br>transplantable murine ascites tumors.'<br>see abstract<br>& PROC. EURES SYMP. MACROPHAGE CANCER,<br>1977<br>pages 142 - 154<br>KEITH, MCBRIDE, STUART, EDS. | 1-7,10,<br>11,13-16   |
| D,A                                                  | WO-A-88 06396 (NEUSHUL) 7 September 1988                                                                                                                                                                                                                                                                                                                                                 |                       |

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB93/01848

## 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:
  
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:

For further information please see form PCT/ISA/206 sent to you 26.01.94.

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.:

1,7(in part), 8,10(in part), 11,13,16

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/GB 93/01848

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|-------------------------------------------|---------------------|----------------------------|---------------------|
| WO-A-8806396                              | 07-09-88            | US-A- 4783446              | 08-11-88            |
|                                           |                     | EP-A- 0349586              | 10-01-90            |
|                                           |                     | JP-T- 1503068              | 19-10-89            |
| -----                                     |                     |                            |                     |