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(71) Applicant *(for all designated States except US)*: **LORANTIS LIMITED** [GB/GB]; 410 Cambridge Science Park, Cambridge CB4 0PE (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **BODMER, Mark, William** [GB/GB]; Lorantis Limited, 307 Cambridge Science Park, Milton Road, Cambridge CB4 0WG (GB). **BRIEND, Emmanuel, Cyrille, Pascal** [FR/GB]; Lorantis Limited, 307 Cambridge Science Park, Milton Road, Cambridge CB4 0WG (GB). **CHAMPION, Brian, Robert** [GB/GB]; Lorantis Limited, 307 Cambridge Science Park, Milton Road, Cambridge CB4 0WG (GB). **LENNARD, Andrew, Christopher** [GB/GB]; Lorantis Limited, 307 Cambridge Science Park, Milton Road, Cambridge CB4 0WG (GB). **MCKENZIE, Grahame, James** [GB/GB]; Lorantis Limited, 307 Cambridge Science Park, Milton Road, Cambridge CB4 0WG (GB). **TUGAL, Tamara** [SK/GB]; Lorantis Limited, 307 Cambridge Science Park, Milton Road, Cambridge CB4 0WG (GB). **WARD, George, Albert** [GB/GB]; Lorantis Limited, 307 Cambridge Science Park, Milton Road, Cambridge CB4 0WG (GB). **YOUNG, Lesley, Lynn** [GB/GB]; Lorantis Limited, 307 Cambridge Science Park, Milton Road, Cambridge CB4 0WG (GB).

(74) Agent: **MALLALIEU, Catherine, Louise**; D. Young & Co., 21 New Fetter Lane, London EC4A 1DA (GB).

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(54) Title: MODULATORS OF THE NOTCH SIGNALLING PATHWAY AND USES THEREOF IN MEDICAL TREATMENT

(57) Abstract: A method is disclosed for therapeutic modulation of Notch signalling by administering a construct comprising a multiplicity of bound, linked or immobilised modulators of Notch signalling.

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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/705 G01N33/68 A61K38/17

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 C07K G01N 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, CHEM ABS Data, EMBASE, MEDLINE, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	HICKS C ET AL: "A SECRETED DELTA1-FC FUSION PROTEIN FUNCTIONS BOTH AS AN ACTIVATOR AND INHIBITOR OF NOTCH1 SIGNALING" JOURNAL OF NEUROSCIENCE RESEARCH, WILEY-LISS, US, vol. 68, no. 6, 15 June 2002 (2002-06-15), pages 655-667, XP009013890 ISSN: 0360-4012	1-7, 14-20, 24,25, 30-35, 41-46, 51,52, 88-90,92
P,Y	the whole document	76-81, 83-85, 99-106, 111-116

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

[X] Patent family members are listed in annex.

° Special categories of cited documents :

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"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	Date of mailing of the international search report
12 November 2003	27/11/2003

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	Armandola, E

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 03/01525

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 913 404 A (ASAHI CHEMICAL IND) 6 May 1999 (1999-05-06)	1-7, 14-20, 24,25, 30-35, 41-46, 51,52, 88-90,92
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A	OSBORNE B ET AL: "Notch and the immune system" IMMUNITY, CELL PRESS, US, vol. 11, no. 6, December 1999 (1999-12), pages 653-663, XP002217474 ISSN: 1074-7613	
A	GRAY G E ET AL: "HUMAN LIGANDS OF THE NOTCH RECEPTOR" AMERICAN JOURNAL OF PATHOLOGY, PHILADELPHIA, PA, US, vol. 154, no. 3, March 1999 (1999-03), pages 785-794, XP000960906 ISSN: 0002-9440	
A	JANG M-S ET AL: "NOTCH SIGNALING AS A TARGET IN MULTIMODALITY CANCER THERAPY" CURRENT OPINION IN MOLECULAR THERAPEUTICS, CURRENT DRUGS, LONDON,, GB, vol. 2, no. 1, February 2000 (2000-02), pages 55-65, XP009013844 ISSN: 1464-8431	

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 03/01525

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	ZLOBIN A ET AL: "TOWARD THE RATIONAL DESIGN OF CELL FATE MODIFIERS: NOTCH SIGNALING AS A TARGET FOR NOVEL BIOPHARMACEUTICALS" CURRENT PHARMACEUTICAL BIOTECHNOLOGY, BENTHAM SCIENCE PUBLISHERS, BOCA RATON,FL, US, vol. 1, no. 1, July 2000 (2000-07), pages 83-106, XP008004456 ISSN: 1389-2010 ---	
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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-98,117-127

Present claims 1-98 and 117-127 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the known Notch ligands (e.g. Deltal, Jagged, Serrate etc.) and to the proteins identified in the application by SEQ. ID. NOs.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

International application No.
PCT/GB 03/01525

INTERNATIONAL SEARCH REPORT

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.: 1-98,117-127
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:
see FURTHER INFORMATION sheet PCT/ISA/210

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:

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
PCT/GB 03/01525

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