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Published:

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- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))

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Previous Correction:

see Notice of 12 March 2009

(54) Title: COMPOSITIONS AND METHODS FOR TREATING TUMORS, FIBROSIS, AND PULMONARY ALVEOLAR PROTEINOSIS

(57) Abstract: The present disclosure provides pharmaceutical compositions and methods useful for modulating angiogenesis and for inhibiting metastasis, tumors, pulmonary alveolar proteinosis, and fibrosis in a mammalian tissue. Pharmaceutical compositions and methods include inhibitors of LOXL2 expression and activity, such as shRNA targeting LOXL2.



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INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2008/000985

A. CLASSIFICATION OF SUBJECT MATTER

INV. C12N15/11 A61K31/713

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)

C12N 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, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PEINADO HECTOR ET AL: "A molecular role for lysyl oxidase-like 2 enzyme in Snail regulation and tumor progression" EMBO JOURNAL, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 24, no. 19, 1 October 2005 (2005-10-01), pages 3446-3458, XP002508336 ISSN: 0261-4189 [retrieved on 2005-08-18] figure 8	1,2, 12-14, 16,17,20
X	US 2007/021365 A1 (ERLER JANINE [US] ET AL) 25 January 2007 (2007-01-25) example 13 ----- -/--	1,2, 12-14, 16,17,20

☒ 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 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

23 February 2009

Date of mailing of the international search report

10/07/2009

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No

PCT/IL2008/000985

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 2007/126457 A (UNIV LELAND STANFORD JUNIOR [US]; ERLER JANINE [US]; GIACCIA AMATO [US] 8 November 2007 (2007-11-08) example 13 -----	1,2, 12-14, 16,17,20
A	FONG SHERI F T ET AL: "Lysyl oxidase-like 2 expression is increased in colon and esophageal tumors and associated with less differentiated colon tumors." GENES, CHROMOSOMES & CANCER JUL 2007, vol. 46, no. 7, 29 March 2007 (2007-03-29), pages 644-655, XP002516214 ISSN: 1045-2257 the whole document -----	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 3-11,15,21-34

The specific sequences of claims 1-34 have, according to PCT Rule 13ter.1.d, not been searched since the Sequence Listing as present in the description does not comply with WIPO Standard ST 25 prescribed in the administrative instructions under Rule 5.2. The Sequence Listing has been furnished neither in paper form nor in machine readable form as provided for in the same instructions and the applicant has not remedied the disclosed deficiencies within the time limit fixed in the invitation pursuant to PCT Rule 13ter.1.a.

Consequently claims 3-11,15, 21-34 have not been searched and SEQ ID NO:2 of claims 1,2,12-14,16-20 is understood as referring to LOXL2 gene.

The applicant's attention is drawn to the fact that 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.2), should the problems which led to the Article 17(2)PCT declaration be overcome.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2008/000985

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.: 3-11, 15, 21-34
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 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:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers 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.:
1-34 (insofar they are searchable)

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-34 (insofar they are searchable)

An RNAi agent against LOXL2 and methods related to cancer or cell growth

2. claims: 35-39

Diagnostic and therapeutic methods related to pulmonary alveolar proteinosis (PAP) involving a LOX inhibitor

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IL2008/000985

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2007021365 A1	25-01-2007	US 2007225242 A1	27-09-2007
WO 2007126457 A	08-11-2007	AU 2007243948 A1	08-11-2007
		CA 2650597 A1	08-11-2007
		EP 2010224 A2	07-01-2009