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(54) Title: USE OF IMMUNOMODULATORY COMPOUNDS FOR THE TREATMENT OF DISORDERS ASSOCIATED WITH ENDOTHELIAL DYSFUNCTION

(57) Abstract: Methods of treating, preventing or managing endothelial dysfunction and other disorders are disclosed. The methods encompass the administration of an immunomodulatory compound provided herein. Further described are methods of treatment using the immunomodulatory compounds in combination with a second active agent. Pharmaceutical compositions and single unit dosage forms suitable for use in the methods provided herein are also disclosed.



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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/012537

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K31/00 A61K31/366 A61K31/454 A61K31/554 A61K45/06
A61P3/00 A61P9/00 A61P13/12 A61P3/10 A61P17/12
A61P37/02

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)

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, EMBASE, CHEM ABS Data, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DAVIGNON J: "The cardioprotective effects of statins" CURRENT ATHEROSCLEROSIS REPORTS 200401 GB, vol. 6, no. 1, January 2004 (2004-01), pages 27-35, XP002515903 ISSN: 1523-3804	1-5,8
Y	the whole document	19-23
X	WO 2005/105088 A (CELGENE CORP [US]; ZELDIS JEROME B [US]) 10 November 2005 (2005-11-10) cited in the application	1-5,8, 13-16, 19,20,23
Y	page 7, lines 4-19 page 4, lines 14-20 page 2, line 31 - page 3, line 2 page 10, lines 14-27	21,22
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☒ 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

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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.
X	US 5 874 448 A (MULLER GEORGE W [US] ET AL) 23 February 1999 (1999-02-23) column 1, lines 6-25 column 2, lines 23-32 claims	2-5, 8, 19, 20, 23
Y	WO 2007/033112 A (CELGENE CORP [US]; VERHELLE DOMINIQUE [US]; CHAN KYLE [US]; BRADY HELE) 22 March 2007 (2007-03-22) cited in the application claims	1-5, 8, 19-23
Y	WO 2005/065455 A (CELGENE CORP [US]; ZELDIS JEROME B [US]; SCHAFER PETER H [US]; FALECK) 21 July 2005 (2005-07-21) cited in the application claims paragraph [0015]	1-5, 8, 19-23
X	US 5 635 517 A (MULLER GEORGE W [US] ET AL) 3 June 1997 (1997-06-03) the whole document	1-5, 8, 17, 18, 21-23
A	KWAK B ET AL: "STATINS AS A NEWLY RECOGNIZED TYPE OF IMMUNOMODULATOR" NATURE MEDICINE, NATURE PUBLISHING GROUP, NEW YORK, NY, US, vol. 12, no. 6, 1 December 2000 (2000-12-01), pages 1399-1402, XP001069419 ISSN: 1078-8956	1-5, 8
P, X	DEBATIN K -M ET AL: "Endothelial progenitor cells for cancer gene therapy" GENE THERAPY 200805 GB, vol. 15, no. 10, May 2008 (2008-05), pages 780-786, XP002515904 ISSN: 0969-7128 1476-5462 abstract	1, 3, 4

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/012537

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.:
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 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.:

see annex

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: 1-3, 13-23 (all partly); 4-5,8

The use of immunomodulators for preventing and treating cardiovascular disorders

2. claims: 1-3, 13-23 (all partly); 6,10,11

The use of immunomodulators for preventing and treating diabetes

3. claims: 1-3, 13-23 (all partly)

The use of immunomodulators for preventing and treating systemic sclerosis

4. claims: 1-3, 13-23 (all partly); 7,9

The use of immunomodulators for preventing and treating chronic renal failure

5. claims: 1-3, 13-23 (all partly); 12

The use of immunomodulators for promoting wound healing

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2008/012537

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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