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(54) Title: NEW PHARMACEUTICAL USES OF STAUROSPORINE DERIVATIVES

(57) Abstract: This application relates to the use of staurosporines derivatives for the curative, palliative or prophylactic treatment of allergic rhinitis, allergic dermatitis, drug allergy or food allergy, angioedema, urticaria, sudden infant death syndrome, bronchopulmonary aspergillosis, multiple sclerosis, or mastocytosis; and to a method of treatment of warm-blooded animals in which a therapeutically effective dose of a compound of a Staurosporine Derivative is administered to a warm-blooded animal suffering from one of the diseases or conditions mentioned above.

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/553 A61P37/08 A61P27/14

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 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, CHEM ABS Data

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P,X	WO 03/065995 A (LYONS JOHN ; SUPERGEN INC (US); RUBINFELD JOSEPH (US)) 14 August 2003 (2003-08-14) claims 33,35,45,53	1,2,4,6
X	WO 99/62537 A (CORNELL RES FOUNDATION INC ; UNIV ROCKEFELLER (US)) 9 December 1999 (1999-12-09) page 5, lines 7-9; claims 12,16,18,26	1,2,6
A	WO 98/48795 A (LILLY CO ELI) 5 November 1998 (1998-11-05) page 3, lines 21,22; claims	1

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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 :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"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	Date of mailing of the international search report
17 January 2005	

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	Veronese, A

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A	EP 0 470 490 A (HOFFMANN LA ROCHE) 12 February 1992 (1992-02-12) page 6, line 55; claim 1	1,2
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Y	KUROSAWA M ET AL: "Effect of staurosporine on histamine release from rat serosal mast cells." ANNALS OF ALLERGY. SEP 1989, vol. 63, no. 3, September 1989 (1989-09), pages 231-234, XP009036192 ISSN: 0003-4738 the whole document	1-3,6,8, 10,11, 13-19
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A	WO 02/080925 A (NOVARTIS AG ; KOIKE KENICHI (JP); NAKAJIMA MOTOWO (JP); KOMIYAMA ATSUS) 17 October 2002 (2002-10-17) See claim 1: treatment of infant death syndrome, bronchopulmonary aspergillosis, mastocytosis, multiple sclerosis.claims 4,5	1-19

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T	OPDAL S H ET AL: "New insight into sudden infant-death syndrome" LANCET THE, LANCET LIMITED. LONDON, GB, vol. 364, no. 9437, 4 September 2004 (2004-09-04), pages 825-826, XP004552551 ISSN: 0140-6736 the whole document	1-3,6,8, 11,19
A	US 4 639 455 A (MOORE LUANA) 27 January 1987 (1987-01-27) See claim 1: prevention of sudden infant death syndrome	1-3,6,8, 11,19
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A	WARK P A ET AL: "Allergic bronchopulmonary aspergillosis: new concepts of pathogenesis and treatment." RESPIROLOGY (CARLTON, VIC.) MAR 2001, vol. 6, no. 1, March 2001 (2001-03), pages 1-7, XP002313470 ISSN: 1323-7799 abstract table 2 See page 4 "Management of allergic bronchopulmonary aspergillosis". page 4, column 1 - page 5, column 2 page 6, column 1	1-3,6,8, 10,11, 13-19
A	GREENBERGER PAUL A: "Clinical aspects of allergic bronchopulmonary aspergillosis." FRONTIERS IN BIOSCIENCE : A JOURNAL AND VIRTUAL LIBRARY. 1 JAN 2003, vol. 8, 1 January 2003 (2003-01-01), pages s119-s127, XP002313471 ISSN: 1093-4715 See page 125: "Approach to treatment of allergic bronchopulmonary aspergillosis"	1-3,6,8, 10,11, 13-19
A	SVIRSHCHEVSKAYA E V ET AL: "Immunotherapy of allergic bronchopulmonary aspergillosis: a clinical and experimental approach." FRONTIERS IN BIOSCIENCE : A JOURNAL AND VIRTUAL LIBRARY. 1 JAN 2003, vol. 8, 1 January 2003 (2003-01-01), pages s92-101, XP002313472 ISSN: 1093-4715 See page 96: "Conclusions" abstract	1-3,6,8, 10,11, 13-19

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A	BRADSHAW D ET AL: "THERAPEUTIC POTENTIAL OF PROTEIN KINASE C INHIBITORS" AGENTS AND ACTIONS, BIRKHAEUSER VERLAG, BASEL, CH, vol. 38, 1993, pages 135-147, XP009034964 ISSN: 0065-4299 abstract See page 138, columns 1,2: "Multiple sclerosis" See page 142, column 1: reference to staurosporine table 1	1-3,6,8, 10,11, 13-19
A	HUDSON S J ET AL: "Intracellular signaling of tumor necrosis factor-alpha in brain microvascular endothelial cells is mediated by a protein tyrosine kinase and protein kinase C-dependent pathway." JOURNAL OF NEUROIMMUNOLOGY. NOV 1996, vol. 70, no. 2, November 1996 (1996-11), pages 199-206, XP002313473 ISSN: 0165-5728 See page 201, column 2 - page 202, column 2, "Results; pages 204-205, "discussion"; figure 3C; and in particular the references to staurosporin	1-3,6,8, 10,11, 13-19
A	JUREWICZ A M ET AL: "Shedding of TNF receptors in multiple sclerosis patients." NEUROLOGY. 22 OCT 1999, vol. 53, no. 7, 22 October 1999 (1999-10-22), pages 1409-1414, XP008041519 ISSN: 0028-3878 See page 1412, second column: "Protein kinase C inhibition" figure 6	1-3,6,8, 10,11, 13-19
E	DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; MORISHITA, TSUYOSHI ET AL: "Drug for nerve regeneration containing glycogen synthase kinase-3 inhibitors" XP002313532 retrieved from STN Database accession no. 2004:902218 abstract	1-3,6,8, 10,11, 13-19

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Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	& WO 2004/091663 A1 (KYOWA HAKKO KOGYO CO., LTD., JAPAN) 28 October 2004 (2004-10-28) -----	
E	DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; KITA, YASUHIRO ET AL: "Remedy for cerebral neurodegenerative diseases using PPAR.delta. agonist" XP002313533 retrieved from STN Database accession no. 2004:927076 abstract & WO 2004/093910 A1 (FUJISAWA PHARMACEUTICAL CO., LTD., JAPAN) 4 November 2004 (2004-11-04) -----	1-3,6,8, 10,11, 13-19
A	LONGLEY B J ET AL: "NEW APPROACHES TO THERAPY FOR MASTOCYTOSIS A CASE FOR TREATMENT WITH KIT KINASE INHIBITORS" HEMATOLOGY - ONCOLOGY CLINICS OF NORTH AMERICA, W.B. SAUNDERS, US, vol. 14, no. 3, June 2000 (2000-06), pages 689-695, XP008010967 ISSN: 0889-8588 the whole document -----	1-19
A	THARP M D: "Mastocytosis" CURRENT PROBLEMS IN DERMATOLOGY 1998 UNITED STATES, vol. 10, no. 5, 1998, pages 181-210, XP009030211 ISSN: 1040-0486 See pages 202-205: " management" -----	1-19

INTERNATIONAL SEARCH REPORT

International application No.
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Box 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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 6,7, 11-16,19 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 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 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. [X] 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.

[X] 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, 2, 3, 6, 8, 10, 11, 13, 14, 15, 16, 17 ,18 ,19 (partial);

   Use of compounds falling in the Markush definition (A) of claim 1 and of formula (I), (II), (III), (VI) of claim 2 in relation to the treatment of allergic rhinitis, allergic dermatitis, drug or food allergy, angioderma and urticaria.

   ---

2. claims: 1, 2, 3, 6, 8, 10, 11, 13, 14, 15, 16, 17 ,18 ,19 (partial);

   Use of compounds falling in the Markush definition (A) of claim 1 and of formula (I), (II), (III), (VI) of claim 2 in relation to the treatment of sudden infant death syndrome.

   ---

3. claims: 1, 2, 3, 6, 8, 10, 11, 13, 14, 15, 16, 17 ,18 ,19 (partial);

   Use of compounds falling in the Markush definition (A) of claim 1 and of formula (I), (II), (III), (VI) of claim 2 in relation to the treatment of bronchopulmonary aspergillosis.

   ---

4. claims: 1, 2, 3, 6, 8, 10, 11, 13, 14, 15, 16, 17 ,18 ,19 (partial);

   Use of compounds falling in the Markush definition (A) of claim 1 and of formula (I), (II), (III), (VI) of claim 2 in relation to the treatment of multiple sclerosis.

   ---

5. claims: 1, 2, 3,4,5 6,7, 8, 10, 11, 13, 14, 15, 16, 17 ,18 ,19 (partial); 9, 12, (complete)

   Use of compounds falling in the Markush definition (A) of claim 1 and of formula (I), (II), (III), (VI) of claim 2 in relation to the treatment of mastocytosis.

   ---

6. claims: 1, 2, 6, 19 (partial);

   Use of compounds falling in the Markush definition (B) and (C) of claim 1 and of formula (V) of claim 2 in relation to the treatment of allergic rhinitis, allergic dermatitis, drug or food allergy, angioderma and urticaria.

   ---

7. claims: 1, 2, 6, 19 (partial);

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use of compounds falling in the Markush definition (B) and (C) of claim 1 and of formula (V) of claim 2 in relation to the treatment of sudden infant death syndrome.

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8. claims: 1, 2, 6, 19 (partial);

Use of compounds falling in the Markush definition (B) and (C) of claim 1 and of formula (V) of claim 2 in relation to the treatment of bronchopulmonary aspergillosis.

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9. claims: 1, 2, 6, 19 (partial);

Use of compounds falling in the Markush definition (B) and (C) of claim 1 and of formula (V) of claim 2 in relation to the treatment of multiple sclerosis.

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10. claims: 1, 2, 4, 5, 6,7, 19 (partial);

Use of compounds falling in the Markush definition (B) and (C) of claim 1 and of formula (V) of claim 2 in relation to the treatment of mastocytosis.

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11. claims: 1, 2, 3, 6, 8, 10, 11, 13, 14, 15, 16, 17 ,18 ,19 (partial);

Use of compounds falling in the Markush definition (D) of claim 1 and of formula (IV) of claim 2 in relation to the treatment of allergic rhinitis, allergic dermatitis, drug or food allergy, angioderma and urticaria.

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12. claims: 1, 2, 3, 6, 8, 10, 11, 13, 14, 15, 16, 17 ,18 ,19 (partial);

Use of compounds falling in the Markush definition (D) of claim 1 and of formula (IV) of claim 2 in relation to the treatment of sudden infant death syndrome.

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13. claims: 1, 2, 3, 6, 8, 10, 11, 13, 14, 15, 16, 17 ,18 ,19 (partial);

Use of compounds falling in the Markush definition (D) of claim 1 and of formula (IV) of claim 2 in relation to the treatment of bronchopulmonary aspergillosis.

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14. claims: 1, 2, 3, 6, 8, 10, 11, 13, 14, 15, 16, 17 ,18 ,19 (partial);

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use of compounds falling in the Markush definition (D) of claim 1 and of formula (IV) of claim 2 in relation to the treatment of multiple sclerosis.

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15. claims: 1, 2, 3, 4, 5, 6, 7, 8, 10, 11, 13, 14, 15, 16, 17 ,18 ,19 (partial);

Use of compounds falling in the Markush definition (D) of claim 1 and of formula (IV) of claim 2 in relation to the treatment of mastocytosis.

INTERNATIONAL SEARCH REPORT

Information on patent family members

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