

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
2 February 2006 (02.02.2006)

PCT

(10) International Publication Number
WO 2006/012256 A3

(51) International Patent Classification:

C07D 211/96 (2006.01) A61K 31/4436 (2006.01)
C07D 405/12 (2006.01) A61K 31/4439 (2006.01)
C07D 401/12 (2006.01) A61K 31/444 (2006.01)
C07D 409/14 (2006.01) A61P 25/00 (2006.01)
A61K 31/445 (2006.01) A61P 25/28 (2006.01)
A61K 31/4433 (2006.01)

60134 (US). **BARRAGUE, Matthieu** [FR/US]; 100 Manhattan Avenue, Apt. 2303, Union City, New Jersey 07030 (US). **GUILES, Joseph, W.** [US/US]; 714 Skywalker Place, Lafayette, CO 80026 (US).

(74) Agents: **NEWMAN, Irving** et al.; sanofi-aventis, Route 202-206, P. O. Box 6800, Bridgewater, New Jersey 08807-0800 (US).

(21) International Application Number:

PCT/US2005/022360

(22) International Filing Date: 24 June 2005 (24.06.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/583,740 29 June 2004 (29.06.2004) US
60/624,946 4 November 2004 (04.11.2004) US

(71) Applicant (for all designated States except US): **AVENTIS PHARMACEUTICALS INC.** [US/US]; 300 Somerset Corporate Boulevard, Bridgewater, New Jersey 08807-2854 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **KOSLEY, JR., Raymond, W.** [US/US]; 659 Cedarbrook Road, Bridgewater, NJ 08807 (US). **BARON, Bruce** [US/US]; 763 Boulevard, Westfield, NJ 07090 (US). **JIMONET, Patrick** [FR/FR]; 13 avenue de Normandie, F-78450 Villepreux (FR). **JURCAK, John, G.** [US/US]; 2431 13th Street, Bethlehem, Pennsylvania 18020 (US). **SHIMSHOCK, Stephen, J.** [US/US]; 13 Banor Drive, Hillsborough, New Jersey 08844 (US). **ZHAO, Xu-Yang** [CN/US]; 7 Decker Lane, Bridgewater, New Jersey 08807 (US). **SHER, Rosy** [US/US]; 13 Kelly Court, Bridgewater, New Jersey 08807 (US). **MUELLER, Paul, J.** [US/US]; 1045 Bloomfield St., Apt. 4, Hoboken, New Jersey 07030 (US). **BEALL, Jennifer** [US/US]; 712 Forrest Avenue, Geneva, Illinois

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv))

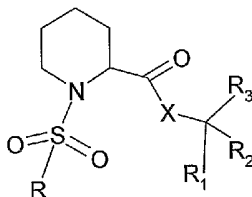
Published:

— with international search report

(88) Date of publication of the international search report:
27 April 2006

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: FKBP BINDING COMPOSITION AND PHARMACEUTICAL USE THEREOF



(I)

(57) Abstract: A composition for binding FKBP proteins is disclosed, along with a method of treating conditions associated with neuronal degeneration, wherein said composition comprises a compound of Formula (I), wherein R, R₁, R₂, R₃ and X are as defined herein.

INTERNATIONAL SEARCH REPORT

International Application No

US2005/022360

A. CLASSIFICATION OF SUBJECT MATTER

C07D211/96 C07D405/12 C07D401/12 C07D409/14 A61K31/445
 A61K31/4433 A61K31/4436 A61K31/4439 A61K31/444 A61P25/00
 A61P25/28

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)

C07D

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, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	I. O. DONKOR ET AL: "Peptidyl Aldehyde Inhibitors of Calpain Incorporating P2-Proline Mimetics" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 13, no. 5, 2003, pages 783-784, XP002362047 page 784, scheme 1, compound 3d	1,2
A	US 6 268 384 B1 (NOVAK PERRY M ET AL) 31 July 2001 (2001-07-31) column 5, line 66 - column 7, line 40; claims 1,10; examples 1,3	1-4,6-9, 11, 17-19,22
A	US 2002/052372 A1 (STEINER JOSEPH P ET AL) 2 May 2002 (2002-05-02) cited in the application page 18, examples no. 54 and 55; claims 1,10 -/-	1,6,11, 21,22



Further documents are listed in the continuation of box C.



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

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

10 January 2006

Date of mailing of the international search report

20/01/2006

Name and mailing address of the ISA

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

Authorized officer

Hass, C

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2005/022360

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	& US 5 696 135 A 9 December 1997 (1997-12-09) cited in the application	
A	& WO 96/40140 A 19 December 1996 (1996-12-19) cited in the application -----	
A	US 2002/052410 A1 (STEINER JOSEPH P ET AL) 2 May 2002 (2002-05-02) cited in the application claims 1,11-14; examples 77-86	1,6,11, 21,22
A	& WO 97/16190 A 9 May 1997 (1997-05-09) cited in the application -----	
A	WO 98/53814 A (MERCK & CO., INC; DURETTE, PHILIPPE, L; HAGMANN, WILLIAM, K; MACCOSS,) 3 December 1998 (1998-12-03) page 1, line 5 - line 21 page 16, line 11 - line 14 claims 1,5,15,18-20 -----	1,6

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/022360

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. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 11-21 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:

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/US2005/022360

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 6268384	B1	31-07-2001	ZA 9807478 A	22-02-1999
US 2002052372	A1	02-05-2002	NONE	
US 5696135	A	09-12-1997	JP 3060373 B2	10-07-2000
			JP 8333256 A	17-12-1996
			LT 98002 A	25-02-1999
			US 5798355 A	25-08-1998
WO 9640140	A	19-12-1996	AU 710423 B2	23-09-1999
			AU 6162296 A	30-12-1996
			BG 102072 A	31-08-1998
			BR 9608485 A	06-07-1999
			CA 2206824 A1	19-12-1996
			CH 689541 A5	15-06-1999
			CZ 9702329 A3	15-07-1998
			DE 19680255 T0	05-06-1997
			DK 125696 A	20-12-1996
			EA 1379 B1	26-02-2001
			EE 9700331 A	15-06-1998
			EP 0777478 A1	11-06-1997
			ES 2138518 A1	01-01-2000
			ES 2166740 A1	16-04-2002
			ES 2194596 A1	16-11-2003
			FI 964137 A	15-01-1997
			GB 2305605 A	16-04-1997
			HK 1013254 A1	16-06-2000
			HU 9900816 A2	28-07-1999
			LU 88834 A1	15-01-1997
			LV 11986 A	20-03-1998
			NO 974290 A	04-12-1997
			NZ 310767 A	24-11-2000
			PL 323381 A1	30-03-1998
			SE 9604097 A	08-12-1996
			SI 9620089 A	30-04-1999
			SK 161097 A3	04-11-1998
			TW 523410 B	11-03-2003
			US 5843960 A	01-12-1998
US 2002052410	A1	02-05-2002	US 2002042377 A1	11-04-2002
WO 9716190	A	09-05-1997	AU 713302 B2	25-11-1999
			AU 6857396 A	22-05-1997
			BG 62596 B1	31-03-2000
			BG 102410 A	30-12-1998
			CA 2236328 A1	09-05-1997
			CZ 9801251 A3	16-12-1998
			EA 1481 B1	23-04-2001
			EE 9800125 A	15-10-1998
			EP 0859614 A1	26-08-1998
			HU 9901752 A2	28-10-1999
			JP 11514643 T	14-12-1999
			LV 12102 A	20-08-1998
			NO 981903 A	30-06-1998
			NZ 316361 A	30-08-1999
			PL 326420 A1	14-09-1998
			SK 55998 A3	11-02-1999

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2005/022360

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9853814	A	03-12-1998	CA 2291778 A1	03-12-1998
			EP 1001764 A1	24-05-2000
			JP 2002512625 T	23-04-2002