

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
8 January 2009 (08.01.2009)

PCT

(10) International Publication Number  
**WO 2009/005646 A3**

(51) International Patent Classification:

C07D 241/04 (2006.01) A61K 31/496 (2006.01)  
C07D 401/06 (2006.01) A61K 31/506 (2006.01)  
C07D 401/14 (2006.01) A61P 3/00 (2006.01)  
C07D 403/12 (2006.01) A61P 9/10 (2006.01)  
C07D 403/14 (2006.01)

Avenue, Teaneck, New Jersey 07666 (US). **CELLY, Chand-  
der, Shekher** [CA/US]; 85 West Street, Colonia, New Jer-  
sey 07067 (US).

(74) Agent: **MACMILLAN, Keith**; Schering-Plough Corpo-  
ration, Patent Department, K-6-1 1990, 2000 Galloping  
Hill Road, Kenilworth, New Jersey 07033-0530 (US).

(21) International Application Number:

PCT/US2008/007868

(22) International Filing Date: 25 June 2008 (25.06.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/946,873 28 June 2007 (28.06.2007) US

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

(71) Applicant (for all designated States except US): **SCHER-  
ING CORPORATION** [US/US]; 2000 Galloping Hill  
Road, Kenilworth, New Jersey 07033-0530 (US).

(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, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL,  
NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG,  
CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(72) Inventors; and

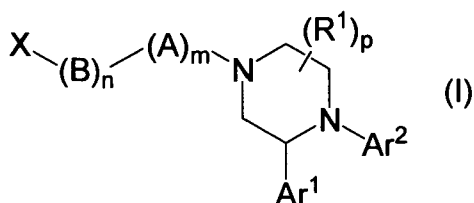
(75) Inventors/Applicants (for US only): **GILBERT, Eric, J.**  
[US/US]; 2119 Gamble Road, Scotch Plains, New Jersey  
07076 (US). **MILLER, Michael, W.** [US/US]; 1862 Lam-  
berts Mill Road, Scotch Plains, New Jersey 07076 (US).  
**SCOTT, Jack, D.** [US/US]; 2089 Westfield Road Circle,  
Scotch Plains, New Jersey 07076 (US). **DEMONG, Du-  
ane, Eugene** [US/US]; 14 Landry Road, Somerset, New  
Jersey 08873 (US). **STAMFORD, Andrew** [AU/US]; 27  
Overlook Road, Chatham Township, New Jersey 07928  
(US). **GREENLEE, William, J.** [US/US]; 115 Herrick

Published:

- with international search report
- before the expiration of the time limit for amending the  
claims and to be republished in the event of receipt of  
amendments

(88) Date of publication of the international search report:  
19 March 2009

(54) Title: SUBSTITUTED PIPERAZINES AS CB1 ANTAGONISTS



(57) Abstract: Compounds of Formula (I) or pharmaceutically accept-  
able salts, solvates, or esters thereof, are useful in treating diseases or  
conditions mediated by CB<sub>1</sub> receptors, such as metabolic syndrome and  
obesity, neuroinflammatory disorders, cognitive disorders and psychosis,  
addiction (e.g., smoking cessation), gastrointestinal disorders, and cardio-  
vascular conditions.

WO 2009/005646 A3

**INTERNATIONAL SEARCH REPORT**

International application No PCT/US2008/007868
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**A. CLASSIFICATION OF SUBJECT MATTER**  
 INV. C07D241/04 C07D401/06 C07D401/14 C07D403/12 C07D403/14  
 A61K31/496 A61K31/506 A61P3/00 A61P9/10

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 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, CHEM ABS Data, BEILSTEIN Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2007/057687 A (VERNALIS R & D LTD [GB]; MONCK NATHANIEL JULIUS THOMAS [GB]; DAVIDSON) 24 May 2007 (2007-05-24) cited in the application  page 14 page 67; claim 1 pages 71-72; claims 36,38	1-27, 43-55, 58-61, 65, 67-112
X	WO 2006/060461 A (SCHERING CORP [US]; GILBERT ERIC J [US]; MILLER MICHAEL W [US]; SCOTT) 8 June 2006 (2006-06-08) cited in the application  page 3 page 307; claim 1 page 313; claim 11 page 377; claims 53,55	1-27, 43-55, 58-61, 65, 67-112
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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  21 October 2008	Date of mailing of the international search report  28/01/2009
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer  Jeanjean, Fabien
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## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2008/007868

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2005/080386 A (ASTRAZENECA AB [SE]; NPS PHARMA INC [US]; ARORA JALAJ [CA]; EDWARDS LO) 1 September 2005 (2005-09-01)  page 86; claim 1	1-27, 43-55, 58-61, 65, 67-112
A	WO 2004/085408 A (MITSUBISHI PHARMA CORP [JP]; SANOFI SYNTHELABO [FR]; WATANABE KAZUTOSH) 7 October 2004 (2004-10-07)  page 346; claim 2	1-27, 43-55, 58-61, 65, 67-112
A	US 5 763 444 A (SMITH DAVID W [US] ET AL) 9 June 1998 (1998-06-09)  column 26; claim 1	1-27, 43-55, 58-61, 65, 67-112
A	EP 0 230 402 A (DOMPE FARMACEUTICI SPA [IT]) 29 July 1987 (1987-07-29)  page 1; claim 1	1-27, 43-55, 58-61, 65, 67-112

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2008/007868

## 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 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.:  
1-27, 43-55, 58-61, 65, 67-112 (all in part)

### 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: 1-27, 43-55, 58-61, 65, 67-112 (all in-part)

directed to compound of formula (I) wherein Ar1 and Ar2 are monocyclic aryl and A is -CO- and its related subject-matter  
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2. claims: 1-27, 43-54, 58-61, 65, 67-68, 70-74, 76-92, 94-112 (all in-part)

directed to compound of formula (I) wherein Ar1 and Ar2 are monocyclic aryl and A is -S(O)2- and its related subject-matter  
---

3. claims: 1-27, 43-54, 58-61, 64-65, 67-68, 70-74, 76-92, 94-112 (all in-part)

directed to compound of formula (I) wherein Ar1 and Ar2 are monocyclic aryl and A is -C(=N-OR2)- and its related subject-matter  
---

4. claims: 1-27, 43-54, 57-63, 65, 67-68, 70-74, 76-112 (all in-part)

directed to compound of formula (I) wherein Ar1 and Ar2 are monocyclic aryl and A is -(C(R2)2)q- and its related subject-matter  
---

5. claims: 1-27, 41-50, 52-54, 58-61, 65, 67-68, 70-74, 76-112 (all in-part)

directed to compound of formula (I) wherein Ar1 and Ar2 are monocyclic aryl and m is 0 and its related subject-matter  
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6. claims: 1-20, 22, 24-25, 41-92, 94-112 (all in-part)

directed to compound of formula (I) wherein Ar1 is a polycyclic aryl and Ar2 is aryl and its related subject-matter  
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7. claims: 1 (part)-22 (part), 24 (part)-27 (part), 28-40, 41 (part)-92 (part), 94 (part)-112 (part)

directed to compound of formula (I) wherein, at least, one of Ar1 and Ar2 is heteroaryl and its related subject-matter  
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## INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2008/007868

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2007057687	A	24-05-2007	EP 1960391 A1	27-08-2008
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