

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
11 September 2009 (11.09.2009)

PCT

(10) International Publication Number  
**WO 2009/109501 A3**

(51) International Patent Classification:

A61K 31/095 (2006.01) A61P 27/02 (2006.01)  
C07D 339/04 (2006.01)

(21) International Application Number:

PCT/EP2009/052252

(22) International Filing Date:

26 February 2009 (26.02.2009)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

MI2008A000382 7 March 2008 (07.03.2008) IT

(71) Applicant (for all designated States except US): **CTG Pharma S.r.l.** [IT/IT]; Viale Gran Sasso, 17, I-20131 Milan (IT).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **DEL SOLDATO, Piero** [IT/IT]; Via Toti, 22, I-20052 Monza (MI) (IT). **SANTUS, Giancarlo** [IT/IT]; Via Zuara, 8, I-20146 Milan (IT).

(74) Agents: **POSTIGLIONE, Ferruccio** et al.; c/o Gregorj S.p.A., Via L. Muratori, 13/b, I-20135 Milan (IT).

(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, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, 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, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, 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).

Published:

- with international search report (Art. 21(3))
- 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))

(88) Date of publication of the international search report:

26 August 2010



WO 2009/109501 A3

(54) Title: OCULAR PHARMACEUTICAL COMPOSITIONS

(57) Abstract: The present invention relates to novel derivatives of ophthalmic compounds for the treatment of ocular diseases.

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2009/052252

**A. CLASSIFICATION OF SUBJECT MATTER**  
INV. A61K31/095 C07D339/04 A61P27/02

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 C07D 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, BIOSIS, EMBASE, WPI 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 2007/101606 A (SULFIDRIS S R L [IT]; DEL SOLDATO PIERO [IT]; SANTUS GIANCARLO [IT]; S) 13 September 2007 (2007-09-13) abstract page 1, line 19 - page 2, line 9 page 4, line 2 - line 14 page 8, line 9 - line 19; claims 1-4,10-13	1, 3, 7-9, 29, 30, 36
X	WO 2006/037623 A (EXPOTREND COMPANY SA [CH]; SPARATORE ANNA [IT] CTG PHARMA S R L [IT]) 13 April 2006 (2006-04-13) abstract page 9, line 14 - page 10, line 17 page 12, line 12 - line 18; claims 1-3	1, 4, 7, 8, 10, 29, 30, 36
	----- -/--	

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

Date of mailing of the international search report

16 February 2010

02/07/2010

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

Hoff, Philippe

## INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2009/052252

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document; with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE REGISTRY 18 January 2001 (2001-01-18), XP002568608 retrieved from STN Database accession no. 314755-82-3 abstract</p>	1,2
Y	<p>US 5 420 120 A (BOLTRALIK JOHN J [US]) 30 May 1995 (1995-05-30)</p> <p>abstract; claims; examples</p>	1,2,4-8, 10-13, 29-32
Y	<p>WO 2008/009127 A (ANTIBE THERAPEUTICS INC [CA]; WALLACE JOHN L [CA]; CIRINO GIUSEPPE [IT]) 24 January 2008 (2008-01-24) abstract page 1, line 9 - line 13 page 2, line 20 - line 24 page 9 - page 10 page 22, line 20 - line 24 page 23, line 1 - line 3 page 24, line 5 - line 13; claims 1-13,25,26</p>	1,2,4-8, 10-13, 29-32
A	<p>FR 1 365 268 A (ROUSSEL UCLAF) 3 July 1964 (1964-07-03) the whole document</p>	1-13, 29-32,36
A	<p>EP 0 117 693 A (UPJOHN CO [US]; TEXAS A &amp; M UNIV SYS [US]) 5 September 1984 (1984-09-05) page 29, compound XI</p>	1-13, 29-32,36
A	<p>MITSUKUCHI, MORIHIRO ET AL: "Studies on topical antiinflammatory agents. III. Synthesis of 17.alpha.-acyloxy-9.alpha.-fluoro-11.beta. -hydroxy-16.beta.-methyl-1,4- pregnadiene-3,20-dione 21-thio derivatives and related compounds" CHEMICAL &amp; PHARMACEUTICAL BULLETIN , 37(12), 3286-93 CODEN: CPBTAL; ISSN: 0009-2363, 1989, XP002568607 table IV</p>	1-13, 29-32,36

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP2009/052252

## 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 all searchable 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.:

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: 1-11,29-32,36 (all partially); 12-13 (completely)

Compounds of general formula (I), wherein A is a corticosteroid and their use in the treatment of ocular diseases.

Process for the synthesis of said compounds.

---

2. claims: 1-11,29-32,36 (all partially); 14-16 (completely)

Compounds of general formula (I), wherein A is a betablocker and their use in the treatment of ocular diseases.

Process for the synthesis of said compounds.

---

3. claims: 1-11,29-32,36 (all partially); 17 (completely)

Compounds of general formula (I), wherein A is a carbonic anhydrase inhibitor and their use in the treatment of ocular diseases.

Process for the synthesis of said compounds.

---

4. claims: 1-11,29-32,36 (all partially); 18 (completely)

Compounds of general formula (I), wherein A is a antimuscarinic and their use in the treatment of ocular diseases.

Process for the synthesis of said compounds.

---

5. claims: 1-11,29-32,36 (all partially); 19-21 (completely)

Compounds of general formula (I), wherein A is a sympathomimetic and their use in the treatment of ocular diseases.

Process for the synthesis of said compounds.

---

6. claims: 1-11,29-32,36 (all partially); 22 (completely)

Compounds of general formula (I), wherein A is a local anesthetic and their use in the treatment of ocular diseases.

Process for the synthesis of said compounds.

---

7. claims: 1-11,29-32,36 (all partially); 23 (completely)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Compounds of general formula (I), wherein A is a antibacterial and their use in the treatment of ocular diseases.  
Process for the synthesis of said compounds.  
---

8. claims: 1-11,29-32,36 (all partially); 24 (completely)

Compounds of general formula (I), wherein A is a antiviral and their use in the treatment of ocular diseases.  
Process for the synthesis of said compounds.  
---

9. claims: 1-11,29-32,36 (all partially); 25 (completely)

Compounds of general formula (I), wherein A is a miotic and their use in the treatment of ocular diseases.  
Process for the synthesis of said compounds.  
---

10. claims: 1-11,29-32,36 (all partially); 26 (completely)

Compounds of general formula (I), wherein A is a antihistaminic and their use in the treatment of ocular diseases.  
Process for the synthesis of said compounds.  
---

11. claims: 1-11,29-32,36 (all partially); 27 (completely)

Compounds of general formula (I), wherein A is a antifungal and their use in the treatment of ocular diseases.  
Process for the synthesis of said compounds.  
---

12. claims: 1-11,29-32,36 (all partially); 28 (completely)

Compounds of general formula (I), wherein A is a neuroprotectant or NMDA receptor antagonist and their use in the treatment of ocular diseases.  
Process for the synthesis of said compounds.  
---

13. claim: 33 (completely)

Use of the compound  
5-(p-hydroxyphenyl)-3H-1,2-dithiol-3-thione) in the treatment of ocular diseases.  
---

14. claim: 34 (completely)

Use of the NSAID derivatives of claim 34 in the treatment of ocular diseases.  
---

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

15. claim: 35 (completely)

Use of the angiotensin antagonist derivatives of claim 35  
in the treatment of ocular diseases.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2009/052252

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2007101606 A	13-09-2007	EP 1832575 A1	12-09-2007
		US 2009017003 A1	15-01-2009
WO 2006037623 A	13-04-2006	EP 1645288 A1	12-04-2006
		EP 1886681 A2	13-02-2008
		US 2009275539 A1	05-11-2009
US 5420120 A	30-05-1995	NONE	
WO 2008009127 A	24-01-2008	AU 2007276621 A1	24-01-2008
		AU 2007276679 A1	24-01-2008
		CA 2658429 A1	24-01-2008
		CA 2658433 A1	24-01-2008
		WO 2008009118 A1	24-01-2008
		EP 2041108 A1	01-04-2009
		EP 2057139 A1	13-05-2009
		JP 2009543811 T	10-12-2009
		JP 2009543813 T	10-12-2009
		KR 20090036115 A	13-04-2009
		KR 20090040428 A	24-04-2009
US 2009306412 A1	10-12-2009		
FR 1365268 A	03-07-1964	NONE	
EP 0117693 A	05-09-1984	CA 1225347 A1	11-08-1987
		EP 0234600 A1	02-09-1987
		FI 840751 A	26-08-1984
		JP 59163566 A	14-09-1984
		US 4614712 A	30-09-1986
		ZA 8309718 A	29-08-1984