(19) World Intellectual Property Organization

International Bureau



(43) International Publication Date 12 April 2007 (12.04.2007)

(10) International Publication Number $WO\ 2007/039125\ A3$

(51) International Patent Classification:

C07C 59/56 (2006.01)

C07C 311/08 (2006.01)

C07C 217/76 (2006.01)

C07C 205/34 (2006.01)

(21) International Application Number:

PCT/EP2006/009184

(22) International Filing Date:

21 September 2006 (21.09.2006)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

0519294.3

21 September 2005 (21.09.2005) GE

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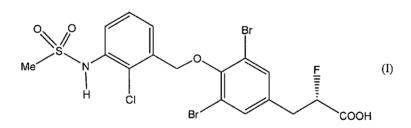
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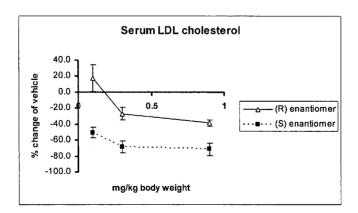
(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, 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, 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, HU, IE, IS, IT, LT, LU, LV, 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).

[Continued on next page]

(54) Title: AN OPTICALLY ACTIVE THYROID RECEPTOR AGONIST AND OPTICALLY ACTIVE KEY INTERMEDIATES IN ITS PRODUCTION





2007/039125 A3

(57) Abstract: The invention provides an optically active form of the compound of formula (I), or a pharmaceutically acceptable ester, amide, solvate or salt thereof, including a salt of such an ester or amide, and a solvate of such an ester, amide or salt; uses of the compound; and methods of preparation of the compound.

WO 2007/039125 A3



Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv))

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:

28 June 2007

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.

International application No PCT/EP2006/009184

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07C59/56 C07C217/76 C07C311/08 C07C205/34 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) C07C 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, WPI Data, PAJ, INSPEC, COMPENDEX C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Category* Citation of document, with indication, where appropriate, of the relevant passages WO 2005/092316 A (KAROBIO AB [SE]; GARCIA X,P 1-11,18,COLLAZO ANNA MARIA [SE]; ERICSSON THOMAS 23-28 ANDER) 6 October 2005 (2005-10-06) compound 55, page 56 page 4, lines 28-30; claims 1-19 page 46, line 25 - page 47, line 19; example 61 A,P WO 2005/092317 A (KAROBIO AB [SE]; GARCIA 1-21.COLLAZO ANA MARIA [SE]; ERICSSON THOMAS 23 - 28ANDERS) 6 October 2005 (2005-10-06) pages 62-63; examples 122-124 description 13, page 67 compound 10, page 69 pages 68-69 Χ Further documents are listed in the continuation of Box C. See patent family annex. Special categories of cited documents: "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 "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 "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to "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) 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 docu-"O" document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. other means *P* document published prior to the international filing date but later than the priority date claimed *&* document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 1 March 2007 11/05/2007 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,

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Seelmann, Marielle

International application No
PCT/EP2006/009184

C(Continua	tion). DOCUMENTS CONSIDERED TO BE RELEVANT	<u> </u>
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Υ	WO 01/36365 A2 (KAROBIO AB [SE]; MALM JOHAN [SE]; LITTEN CHRIS [SE]; APELQVIST THERESA) 25 May 2001 (2001-05-25) in particular example 104 and pages 25-26, scheme 7 with its explanation the whole document	1-21, 23-28
Υ	HAIGH D ET AL: "Anomalous fluorination of 3-aryl-2-hydroxypropanoic esters by diethylaminosulfur trifluoride (DAST)" JOURNAL OF THE CHEMICAL SOCIETY, PERKIN TRANSACTIONS 1, CHEMICAL SOCIETY. LETCHWORTH, GB, no. 24, 1996, pages 2895-2900, XP002153922 ISSN: 0300-922X cited in the application the whole document	1-21, 23-28
Υ	F.F.HUERTA ET AL.: "Dynamic kinetic resolution of alpha-hydroxy acid esters" ORGANIC LETTERS, vol. 2, no. 8, 2000, pages 1037-1040, XP002422791 cited in the application scheme 3, compound 1f table 2, entry 10 table 3, entry 6 conclusions	1-21, 23-28
X	EP 0 887 346 A2 (HOFFMANN LA ROCHE [CH]) 30 December 1998 (1998-12-30) example 5I, page 78claims 1-3,6,7	

International application No. PCT/EP2006/009184

Box II	Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)					
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:					
1. X	Claims Nos.: 22 because they relate to subject matter not required to be searched by this Authority, namely:					
	Although claims 4 and 5 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 of formula (I).					
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 Inte	ernational 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.	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. X	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.: 1-21, 23-28					
Remark	on Protest The additional search fees were accompanied by the applicant's protest. 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: 1-21,23-28

compound of formula (I), production process and medical uses thereof as well as its intermediates of formulae (IIa), (IIIa), (IVaa), (VII), (IX), (XII), (XIII) and (XIV)

2. claim: 22

production of compounds of formulae (XI), (XII), (XIII) and (XIV)

information on patent family members

International application No
PCT/EP2006/009184

Patent document cited in search report		Publication date	Patent family Publication member(s) Publication date		Publication date
WO 2005092316	A	06-10-2005	AU CA CN EP KR	2005226914 A1 2560526 A1 1933826 A 1732532 A1 20060130728 A	06-10-2005 06-10-2005 21-03-2007 20-12-2006 19-12-2006
WO 2005092317	A	06-10-2005	CA EP	2562633 A1 1732533 A1	06-10-2005 20-12-2006
WO 0136365	A2	25-05-2001	AU US US	2666901 A 7005538 B1 2005267206 A1	30-05-2001 28-02-2006 01-12-2005
EP 0887346	A2	30-12-1998	AUU BRA CONN CCK HRUDLLP MOON NO PRUGREW TW	713068 B2 7310298 A 9802201 A 2240136 A1 1515559 A 1515562 A 1203228 A 9801974 A3 1016985 A1 980353 A2 9801357 A2 20463 A 124839 A 2977536 B2 11071353 A 26515 A1 982884 A 330506 A 326959 A1 2218335 C2 72827 A1 9801197 A2 517049 B	25-11-1999 24-12-1998 25-05-1999 23-12-1998 28-07-2004 28-07-2004 30-12-1998 13-01-1999 22-04-2005 30-04-1999 28-09-1999 24-12-1998 28-03-2004 15-11-1999 16-03-1999 20-12-2004 28-12-1998 28-10-1999 04-01-1999 10-12-2003 23-05-2000 18-01-1999 11-01-2003