(19) World Intellectual Property Organization

International Bureau





(43) International Publication Date 8 February 2007 (08.02.2007)

(10) International Publication Number WO 2007/014895 A3

(51) International Patent Classification:

A61K 31/7056 (2006.01) **A61P 3/04** (2006.01) **C07H 17/02** (2006.01) **A61P 3/10** (2006.01)

(21) International Application Number:

PCT/EP2006/064715

(22) International Filing Date: 27 July 2006 (27.07.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

05016390.6 28 July 2005 (28.07.2005) EP

(71) Applicant (for all designated States except DE, US):

BOEHRINGER INGELHEIM INTERNATIONAL
GMBH [DE/DE]; Binger Str. 173, 55216 Ingelheim am
Rhein (DE).

(71) Applicant (for all designated States except US): A.JI-NOMOTO CO., INC. [JP/JP]; 15-1 Kyobashi 1-chome, Chuo-ku, Tokyo 104-8315 (JP).

(71) Applicant (for DE only): BOEHRINGER INGELHEIM PHARMA GMBH & CO. KG [DE/DE]; Binger Str. 173, 55216 Ingelheim Am Rhein (DE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): HIMMELSBACH, Frank [DE/DE]; Ahornweg 16, 88441 Mittelbiberach (DE). MAIER, Roland [DE/DE]; Bodelschwinghstr. 39, 88400 Biberach (DE). EICKELMANN, Peter [DE/DE]; Nelkenweg 9, 88441 Mittelbiberach (DE). THOMAS, Leo [DE/DE]; Georg-Schinbain-Str. 221, 88400 Biberach (DE). BARSOUMIAN, Edward, Leon [US/US]; 18640 Maude Ave, Saratoga, CA 95070 (US). DUGI, Klaus [DE/DE]; Frankenstr. 10, 01309 Dresden (DE). PINNETTI, Sabine [DE/DE]; Rissegger Steige 100, 88400 Biberach (DE). RITTER, Regine [DE/DE]; Wilhelm-Kalle-Str. 2, 65203 Wiesbaden (DE). STREICHER, Ruediger [DE/DE]; Kastanienweg 31, 88400 Biberach

(DE). FUJITA, Koichi [JP/JP]; 1-2-2-c1103, Shinkoyasu, Kanagawa-ku, Yokohama, Kanagawa 221-0013 (JP). HATANAKA, Toshihiro [JP/JP]; 2-80-3-223, Shinmei-cho, Saiwai-ku, Kawasaki-shi, Kanagawa 212-0022 (JP). ISHIDA, Nozomu [JP/JP]; 104 Iwai-cho, Hodogaya-ku, Yokohama, Kanagawa 240-0023 (JP). MAEZONO, Katsumi [JP/JP]; 3-1-15 Yuigahama, Kamakura, Kanagawa 248-0014 (JP). OHSUMI, Koji [JP/JP]; Ajinomoto Campany Apartment A110, Ogura 811, Saiwai-ku, Kawasaki, Kanagawa 212-0054 (JP).

(74) Agents: HAMMANN, Heinz et al.; Binger Str. 173, 55216 Ingelheim Am Rhein (DE).

(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, 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, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, 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, 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).

Published:

with international search report

(88) Date of publication of the international search report: 10 May 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.

(54) Title: METHODS FOR PREVENTING AND TREATING METABOLIC DISORDERS AND NEW PYRAZOLE-O-GLY-COSIDE DERIVATIVES

(57) Abstract: The invention relates to methods for preventing or treating metabolic disorders, for improving glycemic control, for preventing progression from impaired glucose tolerance, insulin resistance and/or from metabolic syndrome to type 2 diabetes mellitus, for preventing or treating of complications of diabetes mellitus, for reducing the weight, for preventing or treating the degeneration of pancreatic beta cells, for treating hyperinsulinemia and insulin resistance and diabetes type 1, in patients in need thereof by administering a pharmaceutical composition comprising a pyrazole-O-glycoside as defined in claim 1, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.



INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2006/064715

		1017112	2000/004/15						
A. CLASSI INV.	FICATION OF SUBJECT MATTER A61K31/7056 C07H17/O2 A61P3/04	4 A61P3/10							
According to	nternational Patent Classification (IPC) or to both national classific	ation and IPC							
B. FIELDS SEARCHED									
	cumentation searched (classification system followed by classificati CO7H	on symbols)							
YOTK	00711								
Documentat	ion searched other than minimum documentation to the extent that	such degriments are included in the file	1de accuelond						
Coodmana	ion obtained that the minimum documentation to the extent that the	ach documents are included. In the he	ius searcheu						
Electronic	ata base consulted during the international search (name of data ba	so and where presting anything							
	ternal, CHEM ABS Data, WPI Data	se and, where practical, search terms	used)						
ri OTii	ternar, chen Abs Data, will bata								
C DOCUME	ENTS CONSIDERED TO BE RELEVANT								
Category*	Citation of document, with indication, where appropriate, of the rel	evant passages	Relevant to claim No.						
	The second of th	orani puoduges	rielevant to claim no.						
Α	WO 2005/021566 A (BOEHRINGER ING	ELHEIM							
	INTERNATIONAL GMBH; BOEHRINGER IN	NGELHEIM							
	PHARMA G) 10 March 2005 (2005-03-	-10)							
χ	EP 1 500 403 A (AJINOMOTO CO., INC) 1-22								
26 January 2005 (2005-01-26)									
	the whole document								
Α	EP 1 364 957 A1 (KISSEI PHARMACEU								
	[JP]) 26 November 2003 (2003-11-2	26)							
Furth	er documents are listed in the continuation of Box C.	X See patent family annex.							
* Special ca	ategories of cited documents :	· · · · · · · · · · · · · · · · · · ·							
"T" later document published after the international filing date or priority date and not in conflict with the application but									
considered to be of particular relevance 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									
which is cited to establish the publication date of another cited to establish the cited to establis									
O document referring to an oral disclosure, use, exhibition or other means 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									
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									
7 -	2 Fohnuany 2007	01/00/0007							
	13 February 2007 21/02/2007								
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 Authorized officer									
	NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl,	Dandili Dundaha	n+						
	Fax: (+31-70) 340-3016	Bardili, Burkhart							

International application No. PCT/EP2006/064715

INTERNATIONAL SEARCH REPORT

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:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
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
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.: 1-22 (parts)
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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-20, 22 (parts)

Compounds, prodrugs, pharmaceutical compositions and medical/pharmaceutical use of 4-benzyl-3-beta-D-glucopyranosyl pyrazole derivatives characterised by a trisubstituted 4-benzyl part, the substituents being selected from fluoro, methyl, methoxy and isopropoxy.

2. claims: 1-22 (parts)

Compounds, prodrugs, pharmaceutical compositions and medical/ pharmaceutical use of 4-benzyl-3-beta-D-glucopyranosyl pyrazole derivatives characterised by a disubstituted 4-benzyl part, the substituents being selected from fluoro and alkyl

3. claims: 1-22 (parts)

Compounds, prodrugs, pharmaceutical compositions and medical/ pharmaceutical use of 4-benzyl-3-beta-D-glucopyranosyl pyrazole derivatives characterised by a disubstituted 4-benzyl part, the substituents being selected from halogen and alkoxy.

4. claims: 1-20, 22 (parts)

Compounds, prodrugs, pharmaceutical compositions and medical/pharmaceutical use of 4-benzyl-3-beta-D-glucopyranosyl pyrazole derivatives characterised by a disubstituted 4-benzyl part, the substituents being selected from halogen

5. claims: 1-13, 16-18, 22 (parts)

Compound, prodrugs thereof, pharmaceutical compositions and medical/ pharmaceutical use of 4-benzyl-3-beta-D-glucopyranosyl pyrazole derivatives characterised by a monosubstituted 4-benzyl part, the substituent being 4-ethinyl.

6. claims: 1-17,21, 22 (parts)

Prodrugs, pharmaceutical compositions and medical/pharmaceutical use of 4-benzyl-3- beta-D-glucopyranosyl pyrazole derivatives characterised by a monosubstituted 4-benzyl part, the substituent being 4-ethyl.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

7. claims: 1-17,21, 22 (parts)

Prodrugs, pharmaceutical compositions and medical/pharmaceutical use of 4-benzyl-3- beta-D-glucopyranosyl pyrazole derivatives characterised by a monosubstituted 4-benzyl part, the substituent being 4-bromo.

8. claims: 5, 21, 22 (parts)

Prodrugs, pharmaceutical compositions and medical/pharmaceutical use of 4-benzyl-3-beta-D-glucopyranosyl pyrazole prodrugs characterised by a monosubstituted 4-benzyl part, the substituent being 4-isopropoxy.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/EP2006/064715

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 2005021566	Α	10-03-2005	CA EP	2539032 1660509		10-03-2005 31-05-2006
EP 1500403	Α	26-01-2005	AU CA WO	2003231517 2484306 03090783	A1	10-11-2003 06-11-2003 06-11-2003
EP 1364957	A1	26-11-2003	CA WO TW US US	2438593 02068439 593329 2006142209 2004132669	A1 B A1	06-09-2002 06-09-2002 21-06-2004 29-06-2006 08-07-2004