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## Declarations under Rule 4.17:

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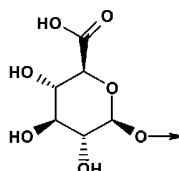
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— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

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10 September 2010

(54) Title: ADAMANTYL O-GLUCURONIDE DERIVATIVES AS INHIBITORS OF DIPEPTIDYL PEPTIDASE IV FOR THE TREATMENT OF DIABETES



(I)

(57) Abstract: The present invention relates to a compound The instant invention relates to a compound of formulae (I A), (I B), (X A), (X B), (Y A) or (Y B), wherein R' represents (formula) and R' represents hydrogen, hydroxy, C<sub>1</sub>-C<sub>7</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, or R<sub>5</sub>R<sub>4</sub>N-CO-O-, where R<sub>4</sub> and R<sub>5</sub> independently are C<sub>1</sub>-C<sub>7</sub>alkyl or phenyl which is unsubstituted or substituted by a substituent selected from C<sub>1</sub>-C<sub>7</sub>alkyl, C<sub>1</sub>-C<sub>7</sub>alkoxy, halogen and trifluoromethyl and where R<sub>4</sub> additionally is hydrogen; or R<sub>4</sub> and R<sub>5</sub> together represent C<sub>3</sub>-C<sub>6</sub>alkylene; in free form or in form of a pharmaceutically acceptable acid addition salt. Compounds of formulae (I A), (I B), (X A), (X B), (Y A) or (Y B) inhibit DPP-IV (dipeptidyl- peptidase-IV) activity. They are therefore indicated for use as pharmaceuticals in inhibiting DPP-IV and in the treatment of conditions mediated by DPP-IV, such as non-insulin- dependent diabetes mellitus, arthritis, obesity, osteoporosis and further conditions of impaired glucose tolerance.

# INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2008/066159

## A. CLASSIFICATION OF SUBJECT MATTER

INV. C07H7/033 C07H15/24 C07H15/26 A61K31/7056 A61P3/10  
ADD.

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)

C07H A61K

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

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2005/012249 A2 (SQUIBB BRISTOL MYERS CO [US]; HAMANN LAWRENCE G [US]; KHANNA ASHISH [U] 10 February 2005 (2005-02-10) claim 2	1
A	WO 00/34241 A1 (NOVARTIS AG [CH]; NOVARTIS ERFIND VERWALT GMBH [AT]; VILLHAUER EDWIN B) 15 June 2000 (2000-06-15) claim 2	1



Further documents are listed in the continuation of Box C.



See patent family annex.

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\*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

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005012249	A2	10-02-2005	AT 444064 T 15-10-2009
		EP 1658066 A2	24-05-2006
		EP 1997489 A1	03-12-2008
		ES 2332275 T3	01-02-2010
		IS 8274 A	31-01-2006
		JP 2007501231 T	25-01-2007
		US 2005239839 A1	27-10-2005
		US 2005228021 A1	13-10-2005
		US 2005038020 A1	17-02-2005
WO 0034241	A1	15-06-2000	AT 307112 T 15-11-2005
		AU 759773 B2	01-05-2003
		AU 1658000 A	26-06-2000
		BR 9915985 A	04-09-2001
		CA 2350609 A1	15-06-2000
		CN 1329593 A	02-01-2002
		CO 5150173 A1	29-04-2002
		CZ 20012028 A3	12-09-2001
		DE 69927844 T2	27-07-2006
		DE 122008000007 I1	17-04-2008
		DE 122008000017 I1	07-08-2008
		DK 1137635 T3	13-02-2006
		EP 1137635 A1	04-10-2001
		ES 2251847 T3	01-05-2006
		HK 1040394 A1	15-09-2006
		HU 0104495 A2	29-04-2002
		ID 28796 A	05-07-2001
		JP 3681110 B2	10-08-2005
		JP 2002531547 T	24-09-2002
		JP 2005112864 A	28-04-2005
		KR 20050047561 A	20-05-2005
		LU 91409 A9	17-03-2008
		LU 91435 A9	09-07-2008
		NL 300333 I1	03-03-2008
		NL 300345 I1	01-07-2008
		NO 2008001 I1	18-02-2008
		NO 2008004 I1	02-06-2008
		NO 20012853 A	07-08-2001
		NZ 511935 A	28-11-2003
		PL 348043 A1	06-05-2002
		SK 7892001 A3	06-11-2001
		TR 200101478 T2	22-10-2001
		TW 509674 B	11-11-2002
		US 6166063 A	26-12-2000
		UY 25843 A1	27-08-2001
		ZA 200104581 A	22-05-2002