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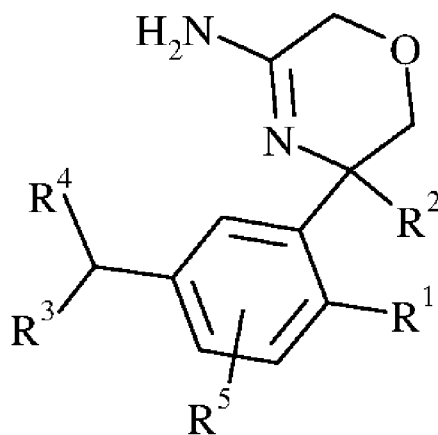
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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, 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, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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[Continued on next page]

(54) Title: 1,4 OXAZINES AS BACE1 AND/OR BACE2 INHIBITORS



(I)

(57) Abstract: The present invention relates to 1,4 Oxazines of formula (I) having BACE1 and/or BACE2 inhibitory activity, their manufacture, pharmaceutical compositions containing them and their use as therapeutically active substances. The active compounds of the present invention are useful in the therapeutic and/or prophylactic treatment of e.g. Alzheimer's disease and type 2 diabetes.



**Published:**

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27 September 2012

- *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))*

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP2012/051481

## 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.:

### 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.

**INTERNATIONAL SEARCH REPORT**

International application No  
PCT/EP2012/051481

A. CLASSIFICATION OF SUBJECT MATTER					
INV.	C07D265/30	C07D413/10	A61K31/5377	A61P3/10	A61P25/28
	A61P7/02	A61P29/00	A61P35/00	A61P9/00	A61P1/00
	A61P19/02				
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) C07D 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 practicable, search terms used)  
EPO-Internal, EMBASE, BIOSIS, 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.
X,P	WO 2011/154431 A1 (JANSSEN PHARMACEUTICA NV [BE]; TRABANCO-SUAREZ ANDRES AVELINO [ES]; RO) 15 December 2011 (2011-12-15) compounds 1-4,8,10,11,23,31-34,36,37,46-48,51-56,58,59,66,67,145,155	1-15,19,21-23,25,28
Y	WO 2011/009943 A1 (NOVARTIS AG [CH]; BADIGER SANGAMESH [IN]; CHEBROLU MURALI [IN]; FREDER) 27 January 2011 (2011-01-27) the whole document	1-28
Y	WO 2009/103626 A1 (HOFFMANN LA ROCHE [CH]; SIENA BIOTECH SPA [IT]; ANDREINI MATTEO [IT];) 27 August 2009 (2009-08-27) the whole document	1-28
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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 invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"&" document member of the same patent family
"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	

Date of the actual completion of the international search <b>3 August 2012</b>	Date of mailing of the international search report <b>10/08/2012</b>
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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 <b>Frelon, Didier</b>
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# INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2012/051481

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 1 942 105 A1 (SHIONOGI & CO [JP]) 9 July 2008 (2008-07-09) the whole document -----	1-28

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/EP2012/051481
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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011154431	A1	15-12-2011	NONE
WO 2011009943	A1	27-01-2011	AR 077328 A1 17-08-2011
		AU 2010274913	A1 02-02-2012
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		US 2012022249	A1 26-01-2012
		WO 2007049532	A1 03-05-2007

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

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

1. claims: 1-28(partially)

compounds of formula I wherein the group R3 -C-R4 is an aromatic group: aryl or heteroaryl  
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2. claims: 1-28(partially)

compounds of formula I wherein the group R3 -C-R4 is an acyclic unsaturated group: alkynyl  
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3. claims: 1-28(partially)

compounds of formula I wherein the group R3 -C-R4 is a non-aromatic cyclic group: cycloalkyl or heterocyclyl  
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