

Title (en)  
DERIVATIVES OF 1-OXO-1,2-DIHYDROISOQUINOLINE-5-CARBOXAMIDES AND OF 4-OXO-3,4-DIHYDROQUINAZOLINE-8-CARBOXAMIDES, PREPARATION THEREOF AND APPLICATION THEREOF IN THERAPEUTICS

Title (de)  
DERIVATE VON 1-OXO-1,2-DIHYDROISOCHINOLIN-5-CARBOXAMIDEN UND 4-OXO-3,4-DIHYDROCHINAZOLIN-8-CARBOXAMIDEN, IHRE HERSTELLUNG UND IHRE ANWENDUNG IN THERAPEUTIKA

Title (fr)  
DÉRIVÉS DE 1-OXO-1,2-DIHYDROISOQUINOLEINE-5-CARBOXAMIDES ET DE 4-OXO-3,4-DIHYDROQUINAZOLINE-8-CARBOXAMIDES, LEUR PRÉPARATION ET LEUR APPLICATION EN THÉRAPEUTIQUE

Publication  
**EP 2185523 A2 20100519 (FR)**

Application  
**EP 08835688 A 20080725**

Priority  

- FR 2008001109 W 20080725
- FR 0705500 A 20070727

Abstract (en)  

[origin: FR2919286A1] Dihydroquinazoline- or dihydroisoquinoline carboxamide compounds (I) and their base or acid addition salts, hydrates or solvates are new. Dihydroquinazoline- or dihydroisoquinoline carboxamide compounds of formula (I) and their base or acid addition salts, hydrates or solvates are new. R 1>H, 1-10C alkyl, 3-7C cycloalkyl, (CH 2) n-(1-6C)alkenyl, (CH 2) n-(1-6C)alkynyl, 1-6C alkyl-Z-(1-6C alkyl), aryl or aralkyl (all optionally substituted by halo, 1-6C alkyl, 3-7C cycloalkyl, halo(1-6C)alkoxy, NR 7>R 8>, nitro, cyano, OR, COOR, CONR 7>R 8>, S(O) mNR 7>R 8>or aryl), COOR or S(O) mR; Z : Heteroatom comprising O, N or S(O) m; R 2>halo(1-6C)alkyl, halo(1-6C)alkoxy, OH, 1-6C alkoxy, NO 2, CN, NH 2, NR 7>R 8>, COOR, CONR 7>R 8>, OCO(1-6C)alkyl, S(O) mNR 7>R 8>or aryl (all optionally substituted by one or more halo, 1-6C alkyl, 3-7C cycloalkyl, halo(1-6C)alkyl, (1-6C)alkoxy, halo(1-6C)alkoxy, NR 7>R 8>, NO 2, CN, OR, COOR, CONR 7>R 8>or S(O) mNR 7>R 8>), H (preferred), halo, 1-6C alkyl, 3-7C cycloalkyl, (1-6C)alkenyl, (1-6C)alkynyl or 1-6C alkyl-Z-(1-6C alkyl); R 3>CF 3; either R 4>, R 5>H; or CR 4>R 5>ring containing of 3-6 carbon atoms (optionally saturated and optionally containing 0-1 heteroatom comprising O, N or S); R 6>H, halo, 1-6C alkyl, 3-7C cycloalkyl, 3-7C cycloalkyl-1-6C alkyl, halo-1-6C alkyl, NO 2, NH 2, NR 7>R 8>, COOR, NR 7>(SO 2)R 8>, CONR 7>R 8>or aryl (all optionally substituted by one or more groups of halo, 1-6C alkyl, 1-6C alkoxy or CN); either R 7>, R 8>, R : H, 1-6C alkyl, 3-7C cycloalkyl, 3-7C cycloalkyl-1-6C alkyl, aryl or aryl(1-6C)alkylene; or R 7>R 8>ring containing 5-7 carbon atoms (optionally saturated and substituted by heteroatom of O, N or S(O) m); X : C or N; m : 0-2; and n : 1-6. Where the: carbon carrying the benzyl substituted by R2 is absolute configuration S; and carbon carrying the hydroxyl is absolute configuration R. [Image] ACTIVITY : Neuroprotective; Nootropic; Antiparkinsonian; Cerebroprotective; Vasotropic; Anticonvulsant; Antimigraine; Antidepressant; Tranquilizer; Antiarteriosclerotic; Cytostatic. MECHANISM OF ACTION : Beta-secretase inhibitor. The ability of (I) to inhibit beta-secretase was tested using fluorescence resonance energy transfer assay. The result showed that N-[(1S,2R)-1-benzyl-2-hydroxy-3-[[3-(trifluoromethyl)benzyl]amino]propyl]-4-oxo-3-(1-propylbutyl)-3,4-dihydroquinazoline-8-carboxamide exhibited an IC 50 value of 0.83-2.6 mu M.

IPC 8 full level  
**C07D 217/24** (2006.01); **A61K 31/472** (2006.01); **A61K 31/498** (2006.01); **A61K 31/517** (2006.01); **A61P 9/00** (2006.01); **A61P 25/00** (2006.01); **A61P 35/00** (2006.01); **C07D 239/88** (2006.01)

CPC (source: EP US)  
**A61P 9/00** (2017.12 - EP); **A61P 9/10** (2017.12 - EP); **A61P 21/00** (2017.12 - EP); **A61P 25/00** (2017.12 - EP); **A61P 25/02** (2017.12 - EP); **A61P 25/06** (2017.12 - EP); **A61P 25/14** (2017.12 - EP); **A61P 25/16** (2017.12 - EP); **A61P 25/22** (2017.12 - EP); **A61P 25/24** (2017.12 - EP); **A61P 25/28** (2017.12 - EP); **A61P 35/00** (2017.12 - EP); **A61P 43/00** (2017.12 - EP); **C07D 217/24** (2013.01 - EP US); **C07D 239/88** (2013.01 - EP US)

Citation (search report)  
See references of WO 2009044018A2

Designated contracting state (EPC)  
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MT NL NO PL PT RO SE SI SK TR

Designated extension state (EPC)  
AL BA MK RS

DOCDB simple family (publication)  
**FR 2919286 A1 20090130**; AU 2008306762 A1 20090409; BR PI0814177 A2 20150120; CA 2694313 A1 20090409; CN 101790518 A 20100728; CO 6290668 A2 20110620; EA 201070196 A1 20100830; EP 2185523 A2 20100519; JP 2010534640 A 20101111; KR 20100047294 A 20100507; MA 31629 B1 20100802; MX 2010001081 A 20100324; NZ 582995 A 20120427; US 2010197706 A1 20100805; US 8030320 B2 20111004; WO 2009044018 A2 20090409; WO 2009044018 A3 20090618; WO 2009044018 A9 20101014; ZA 201000583 B 20110428

DOCDB simple family (application)  
**FR 0705500 A 20070727**; AU 2008306762 A 20080725; BR PI0814177 A 20080725; CA 2694313 A 20080725; CN 200880104537 A 20080725; CO 10007694 A 20100126; EA 201070196 A 20080725; EP 08835688 A 20080725; FR 2008001109 W 20080725; JP 2010517452 A 20080725; KR 20107004332 A 20080725; MA 32646 A 20100224; MX 2010001081 A 20080725; NZ 58299508 A 20080725; US 69359810 A 20100126; ZA 201000583 A 20100126