

## 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 µM.

## IPC 8 full level

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## 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)

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## Designated contracting state (EPC)

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