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C07D 249/10 (2006.01) **A61K 31/4196** (2006.01)
C07D 263/34 (2006.01) **A61K 31/421** (2006.01)
C07D 271/06 (2006.01) **A61K 31/4245** (2006.01)
C07D 271/10 (2006.01) **A61K 31/433** (2006.01)
C07D 277/32 (2006.01) **A61P 9/00** (2006.01)
C07D 285/08 (2006.01) **A61P 11/00** (2006.01)
C07D 307/68 (2006.01) **A61P 37/00** (2006.01)
A61K 31/341 (2006.01) **A61P 25/28** (2006.01)

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English

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(74) Agent: **THEN, Johann**; K 801, Sanofi-Aventis Deutschland GmbH, Patents Germany, Industriepark Höchst, Geb. K 801, 65926 Frankfurt am Main (DE).

(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, BN, 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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Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

Published:

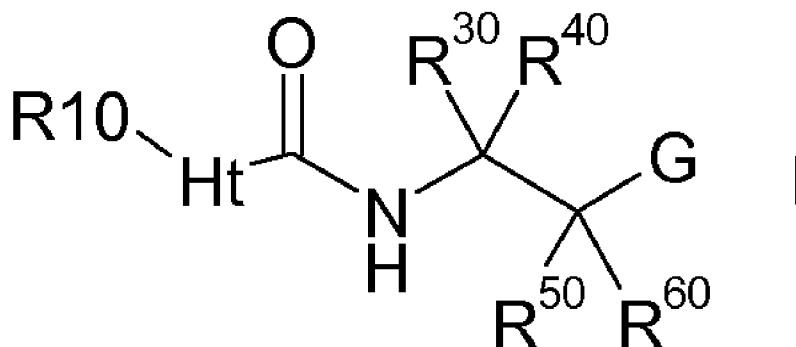
— with international search report (Art. 21(3))

— 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))

(88) Date of publication of the international search report:

4 April 2013

(54) Title: 3-HETEROAROYLAMINO-PROPIONIC ACID DERIVATIVES AND THEIR USE AS PHARMACEUTICALS



(57) Abstract: The present invention relates to compounds of the formula I, wherein Ht, G, R¹⁰, R³⁰, R⁴⁰, R⁵⁰ and R⁶⁰ have the meanings indicated in the claims, which are valuable pharmaceutical active compounds. They are inhibitors of the protease cathepsin A, and are useful for the treatment of diseases such as atherosclerosis, heart failure, renal diseases, liver diseases or inflammatory diseases, for example. The invention furthermore relates to processes for the preparation of the compounds of the formula I, their use and pharmaceutical compositions comprising them.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2012/064628

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D249/10 C07D263/34 C07D271/06 C07D271/10 C07D277/32
C07D285/08 C07D307/68 A61K31/341 A61K31/4196 A61K31/421
A61K31/4245 A61K31/433

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 A61P

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, CHEM ABS Data, WPI Data

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X	US 2007/213302 A1 (MCELROY JOHN FRANCIS [US] ET AL) 13 September 2007 (2007-09-13) table A, compound A6; table B, compound B2; table 5a, compounds 59, 60; table 6a, compound 59; paragraph 14; claims 1, 9, 12-17 -----	1,2,8-11
X	US 2010/022599 A1 (CHOI SEOK-KI [US] ET AL) 28 January 2010 (2010-01-28) claims 1,27; examples 11-15 ----- -/-	1,9-11



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"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)

"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

"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

"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

"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

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Date of the actual completion of the international search

18 January 2013

Date of mailing of the international search report

30/01/2013

Name and mailing address of the ISA/

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Rufet, Jacques

INTERNATIONAL SEARCH REPORT

International application No

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X	WO 2010/136493 A1 (NOVARTIS AG [CH]; COPPOLA GARY MARK [US]; IWAKI YUKI [US]; KARKI RAJES) 2 December 2010 (2010-12-02) examples 4-6, 4-7, 4-10, 4-15, 4-18, 4-30, 4-31, 4-32, 4-34 to 4-37, 11-16, 11-17, 11-29, 11-31, 11-32, 11-35 to 11-37; claims 1,16-18; examples 5-46, 5-57 -----	1,9-11
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A	WO 2011/011232 A1 (THERAVANCE INC [US]; FATHEREE PAUL R [US]; HUDSON RYAN [US]; MCKINNELL) 27 January 2011 (2011-01-27) page 57 - page 70; claims 1-17 -----	1-11
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International application No

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X	WO 2008/124838 A1 (UNIV MARYLAND [US]; TOMKINSON ALAN E [US]; CHEN XI [US]; DZIEGIELEWSKA) 16 October 2008 (2008-10-16) abstract; page 93, compound 207 -----	1,2
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X	EP 1 493 740 A1 (WARNER LAMBERT CO [US]) 5 January 2005 (2005-01-05) claims 1-19; examples 4,5,7 -----	1-6,8-11
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X	WO 99/23063 A1 (RHONE POULENC RORER LTD [GB]; ASTLES PETER CHARLES [GB]; CLARK DAVID E) 14 May 1999 (1999-05-14) page 91, paragraph 8 -----	1,2
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International application No

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	WO 98/29387 A1 (AGROGENE LTD [IL]; COHEN YIGAL [IL]; KORAT MOSHE [IL]) 9 July 1998 (1998-07-09) page 5, line 3 - line 4 -----	1,2
X	DUBLANCHET A C ET AL: "Structure-based design and synthesis of novel non-zinc chelating MMP-12 inhibitors", BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 15, no. 16, 15 August 2005 (2005-08-15), pages 3787-3790, XP025314160, PERGAMON, ELSEVIER SCIENCE, GB ISSN: 0960-894X, DOI: 10.1016/J.BMCL.2005.05.079 [retrieved on 2005-08-15] page 3787; table 3 -----	1-6,8-11
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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2012/064628

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2012/064628

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2012/064628

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE REGISTRY [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 16 March 2008 (2008-03-16), XP002669671, retrieved from STN Database accession no. 1008348-72-8 abstract	1,2
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X	----- WO 2009/028280 A1 (MITSUI CHEMICALS INC [JP]; CHIBA YUTAKA [JP]; KOUNO TOSHIYUKI [JP]; SH) 5 March 2009 (2009-03-05) page 25, formula (7); page 29, compound 140	1,2
X	----- WO 2011/005674 A1 (THERAVANCE INC [US]; BLAIR BROOKE [US]; FATHEREE PAUL R [US]; FLEURY M) 13 January 2011 (2011-01-13) claims 1-14,17; examples 1,2,4-7,10-24 -----	1-11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2012/064628

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-11(partially)

Compounds according to formula (I) wherein Ht is a (1,2,4)-oxadiazole ring

2. claims: 1-11(partially)

Compounds according to formula (I) wherein Ht is an oxazole ring

3. claims: 1-11(partially)

Compounds according to formula (I) wherein Ht is a furan ring

4. claims: 1-11(partially)

Compounds according to formula (I) wherein Ht is a thiophene ring

5. claims: 1-11(partially)

Compounds according to formula (I) wherein Ht is a (1,2,4)-thiodiazole ring

6. claims: 1-11(partially)

Compounds according to formula (I) wherein Ht is (1,2,4)-triazole ring

7. claims: 1-11(partially)

Compounds according to formula (I) wherein Ht is pyrazole ring

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2012/064628

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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