

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
30 November 2006 (30.11.2006)

PCT

(10) International Publication Number
WO 2006/128184 A3

(51) International Patent Classification:

C07D 487/04 (2006.01) **A61P 19/00** (2006.01)
A61K 31/519 (2006.01)

(21) International Application Number:

PCT/US2006/020970

(22) International Filing Date: 22 May 2006 (22.05.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/683,470	20 May 2005 (20.05.2005)	US
60/706,465	8 August 2005 (08.08.2005)	US
60/734,991	9 November 2005 (09.11.2005)	US

(71) Applicant (for all designated States except US): **ALAN-TOS-PHARMACEUTICALS, INC.** [US/US]; RIVERSIDE TECHNOLOGY CENTER, 840 Memorial Drive, Cambridge, MA 02139 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **STEENECK, Christoph** [DE/DE]; Schulstr. 8, 69221 Dossenheim XX (DE). **GEGE, Christian** [DE/DE]; Elsenzstr. 7, 69256 Mauer XX (DE). **RICHTER, Frank** [DE/DE]; Meuhlingstr. 15, 69121 Handschuhsheim XX (DE). **HOCHGUERTEL, Matthias** [DE/DE]; Dossenheimer Weg 53, D-69198 Schriesheim XX (DE). **FEURSTEIN, Tim** [DE/DE]; Kurt-lindemann-strasse 48, D-69151 Neckargemuend XX (DE). **BLUHM, Harald** [DE/DE]; Bergstr. 30c, 69221 Dossenheim XX (DE). **SUCHOLEIKI, Irving** [US/US]; 225 Mystic Valley Parkway, Winchester, MA 01890 (US). **BOER, Jurgen** [DE/DE]; Albrechtstrasse 34, D-65185 Wiesbaden XX (DE). **WU, Xinyuan** [CN/US]; 935 Washington Street, #14, Newton, MA 02460 (US). **SCHNEIDER, Matthias** [DE/DE]; Adalbert-stifter-str. 8, 69221 Dossenheim XX (DE). **NOLTE, Bert** [DE/DE]; Hoehenweg 42, 69250 Schoenau (DE). **GALLAGHER, Brian** [US/US]; 28 Orchard Street, Merrimac, MA 01860 (US). **VAN VELDHUIZEN, Joshua** [US/US]; 51 Addington Road, #2, Brookline, MA

02445 (US). **DENG, Hongbo** [CN/US]; 178 Woodland Road, Southborough, MA 01772 (US). **ESSERS, Michael** [DE/DE]; Ziegelhaeuser Strasse 80, 69250 Schoenau (DE). **KROTH, Heiko** [DE/DE]; Marie-Curie-Weg 3, 69181 Leimen (DE). **KIELY, Andrew** [US/US]; 21 Standish Street, Newton, MA 02461 (US). **POWERS, Timothy** [US/US]; 288 Commonwealth Avenue #4, Boston, MA 02115 (US). **TAVERAS, Arthur, G.** [US/US]; 6 Joslin Lane, Southborough, MA 01772 (US).

(74) Agent: **SCOLA, Daniel, A., Jr.**; HOFFMANN & BARON, LLP, 6900 Jericho Turnpike, Syosset, NY 11791 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(88) Date of publication of the international search report:
8 March 2007

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: PYRIMIDINE OR TRIAZINE FUSED BICYCLIC METALLOPROTEASE INHIBITORS

(57) Abstract: The present invention relates generally to amide group containing pharmaceutical agents, and in particular, to amide containing heterobicyclic metalloprotease inhibitor compounds. More particularly, the present invention provides a new class of heterobicyclic MMP-13 inhibiting compounds, that exhibit an increased potency in relation to currently known MMP-13 inhibitors.

WO 2006/128184 A3

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/020970

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D487/04 A61K31/519 A61P19/00

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

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, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/052315 A (MERCK & CO INC [US]; FRALEY MARK E [US]) 24 June 2004 (2004-06-24) the whole document	1, 18, 31, 106, 107
E	WO 2006/083454 A (ALANTOS PHARMACEUTICALS INC [US]; POWERS TIMOTHY [US]; STEENECK CHRIST) 10 August 2006 (2006-08-10) the whole document	1-142
A	WO 2004/041788 A (AVENTIS PHARMA GMBH [DE]) 21 May 2004 (2004-05-21) the whole document	1-142
A	WO 02/064571 A (WARNER LAMBERT CO [US]; BARVIAN NICOLE CHANTEL [US]; PATT WILLIAM CHES) 22 August 2002 (2002-08-22) the whole document	1-142
----- -/-		

☒ 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 document 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.

"&" document member of the same patent family

Date of the actual completion of the international search

9 November 2006

Date of mailing of the international search report

15/11/2006

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Von Daacke, Axel

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/020970

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2004/014354 A (WARNER LAMBERT CO [US]; ROARK WILLIAM HOWARD [US]) 19 February 2004 (2004-02-19) the whole document -----	1-142
A	WO 02/064595 A (WARNER LAMBERT CO [US]; ANDRIANJARA CHARLES [FR]; JACOBELLI HENRY [FR]) 22 August 2002 (2002-08-22) the whole document -----	1-142
A	WO 2004/014916 A (WARNER LAMBERT CO [US]; WILSON MICHAEL WILLIAM [US]) 19 February 2004 (2004-02-19) the whole document -----	1-142

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/020970

Box 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:

Although claims 109-129 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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 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:

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 fee, this Authority did not invite payment of any additional fee.
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.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/020970

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 2004052315	A	24-06-2004	AU 2003299651 A1	30-06-2004
WO 2006083454	A	10-08-2006	NONE	
WO 2004041788	A	21-05-2004	AU 2003301847 A1	07-06-2004
			BR 0315055 A	16-08-2005
			CA 2504153 A1	21-05-2004
			EP 1560815 A1	10-08-2005
			JP 2006513158 T	20-04-2006
			MA 27412 A1	01-06-2005
			MX PA05004365 A	05-07-2005
WO 02064571	A	22-08-2002	BR 0207209 A	27-01-2004
			CA 2433772 A1	22-08-2002
			EP 1368323 A1	10-12-2003
			JP 2004518723 T	24-06-2004
			MX PA03004920 A	05-09-2003
WO 2004014354	A	19-02-2004	AU 2003249535 A1	25-02-2004
WO 02064595	A	22-08-2002	AT 294805 T	15-05-2005
			BR 0207270 A	10-02-2004
			CA 2437588 A1	22-08-2002
			DE 60203995 D1	09-06-2005
			DE 60203995 T2	22-09-2005
			EP 1362048 A1	19-11-2003
			ES 2239216 T3	16-09-2005
			JP 2004521908 T	22-07-2004
			MX PA03007249 A	14-02-2005
WO 2004014916	A	19-02-2004	AU 2003253165 A1	25-02-2004