

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
10 November 2005 (10.11.2005)

PCT

(10) International Publication Number
WO 2005/105760 A1

(51) International Patent Classification⁷: **C07D 239/90**,
401/12, 405/12, 409/14, 413/14, 405/14, 495/04, 471/04,
217/26, 487/04, 491/04, 498/04, A61K 31/505, A61P
19/02

Osaka-shi, Osaka, 5328686 (JP). **SATO, Kenjiro** [JP/JP];
c/o TAKEDA PHARMACEUTICAL COMPANY LIM-
ITED, 17-85, Jusohonmachi 2-chome, Yodogawa-ku,
Osaka-shi, Osaka, 5328686 (JP).

(21) International Application Number:
PCT/JP2005/008549

(74) Agent: **TAKASHIMA, Hajime**; Meiji Yasuda Seimei Os-
aka Midosuji Bldg., 1-1, Fushimimachi 4-chome, Chuo-ku,
Osaka-shi, Osaka 5410044 (JP).

(22) International Filing Date: 28 April 2005 (28.04.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
2004-135596 30 April 2004 (30.04.2004) JP

(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, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, MZ, NA, 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.

(71) Applicant (for all designated States except US): **TAKEDA
PHARMACEUTICAL COMPANY LIMITED** [JP/JP];
1-1, Doshomachi 4-chome, Chuo-ku, Osaka-shi, Osaka,
5410045 (JP).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **TERAUCHI, Jun**
[JP/JP]; c/o TAKEDA PHARMACEUTICAL COMPANY
LIMITED, 17-85, Jusohonmachi 2-chome, Yodogawa-ku,
Osaka-shi, Osaka, 5328686 (JP). **KUNO, Haruhiko**
[JP/JP]; c/o TAKEDA PHARMACEUTICAL COMPANY
LIMITED, 17-85, Jusohonmachi 2-chome, Yodogawa-ku,
Osaka-shi, Osaka, 5328686 (JP). **NARA, Hiroshi** [JP/JP];
c/o TAKEDA PHARMACEUTICAL COMPANY LIM-
ITED, 17-85, Jusohonmachi 2-chome, Yodogawa-ku,
Osaka-shi, Osaka, 5328686 (JP). **OKI, Hideyuki** [JP/JP];
c/o TAKEDA PHARMACEUTICAL COMPANY LIM-
ITED, 17-85, Jusohonmachi 2-chome, Yodogawa-ku,

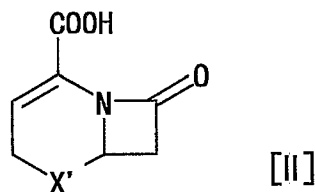
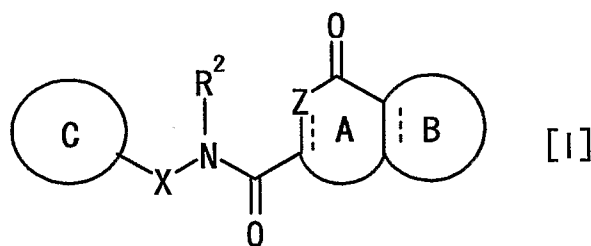
(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, 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

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

(54) Title: HETEROCYCLIC AMIDE COMPOUND AND USE THEREOF AS AN MMP-13 INHIBITOR



(57) Abstract: The present invention provides a novel
amide derivative having a matrix metalloproteinase inhibitory
activity, and useful as a pharmaceutical agent, which is a
compound represented by the formula (I) wherein ring A is
an optionally substituted, nitrogen-containing heterocycle,
ring B is an optionally substituted monocyclic homocycle
or an optionally substituted monocyclic heterocycle, Z is N
or NR¹ (R¹ is a hydrogen atom or an optionally substituted
hydrocarbon group), --- is a single bond or a double bond, R²
is a hydrogen atom or an optionally substituted hydrocarbon
group, X is an optionally substituted spacer having 1 to 6
atoms, ring C is (1) an optionally substituted homocycle
or (2) an optionally substituted heterocycle other than a
ring represented by (II) (X' is S, O, SO, or CH₂), and at
least one of ring B and ring C has substituent(s), provided
that N-[(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylben-
zyl)amino]-2-hydroxypropyl]-5,6-dimethyl-4-oxo-1,4-di-
hydrothieno[2,3-d]pyrimidine-2-carboxamide is excluded, or
a salt thereof.