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 C07D 207/10 (2006.01) C07D 211/56 (2006.01)  
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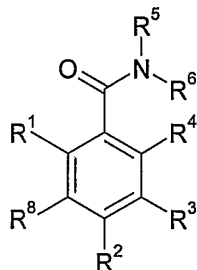
## Published:

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30 November 2006

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: HYDROXYBENZAMIDE DERIVATIVES AND THEIR USE AS INHIBITORS OF HSP90



(I)

an acyclic C<sub>1-5</sub> hydrocarbyl group or a monocyclic carbocyclic or heterocyclic group having 3 to 7 ring members; halogen; cyano; hydroxy; amino; and mono- or di-C<sub>1-5</sub> hydrocarbyl-amino, wherein the acyclic C<sub>1-5</sub> hydrocarbyl group and the mono and di-C<sub>1-5</sub> hydrocarbylamino moieties in each instance are optionally substituted by one or more substituents selected from hydroxy, halogen, C<sub>1-2</sub> alkoxy, amino, mono- and di-C<sub>1-2</sub> alkylamino, and aryl and heteroaryl groups of 5 to 12 ring members; or R<sup>3</sup> and R<sup>4</sup> together form a monocyclic carbocyclic or heterocyclic ring of 5 to 7 ring members; and R<sup>7</sup> and R<sup>8</sup> are as defined in the claims.

(57) Abstract: The invention provides a compound for use as an inhibitor of Hsp90, the compound having the formula (I); or salts, tautomers, solvates and N-oxides thereof; wherein R<sup>1</sup> is hydroxy or hydrogen; R<sup>2</sup> is hydroxy; methoxy or hydroxy; provided that at least one of R<sup>1</sup> and R<sup>2</sup> is hydroxy; R<sup>3</sup> is selected from hydrogen; halogen; cyano; C<sub>1-5</sub> hydrocarbyl and C<sub>1-5</sub> hydrocarbyloxy; wherein the C<sub>1-5</sub> hydrocarbyl and C<sub>1-5</sub> hydrocarbyloxy moieties are each optionally substituted by one or more substituents selected from hydroxy, halogen, C<sub>1-2</sub> alkoxy, amino, mono- and di-C<sub>1-2</sub> alkylamino, and aryl and heteroaryl groups of 5 to 12 ring members; R<sup>4</sup> is selected from hydrogen; a group -(O)<sub>n</sub>-R<sup>7</sup> where n is 0 or 1 and R<sup>7</sup> is

WO 2006/109075 A3

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/GB2006/001358

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>							
INV.	A61K31/401	A61K31/445	A61K31/5375	A61K31/166	C07C233/65		
	C07C233/66	C07D207/10	C07D211/34	C07D295/02	C07D309/14		
	C07D265/30	C07D295/18	C07D211/42	C07D211/22	C07D211/56		
According to International Patent Classification (IPC) or to both national classification and IPC							
<b>B. FIELDS SEARCHED</b>							
Minimum documentation searched (classification system followed by classification symbols) A61K C07C 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, CHEM ABS Data, WPI Data, PAJ							
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>							
Category*	Citation of document, with indication, where appropriate, of the relevant passages				Relevant to claim No.		
X	CAI, XIONGWEI ET AL: "Regiospecific synthesis of alkylphenanthrenes using a combined directed ortho and remote metalation-Suzuki-Miyaura cross coupling strategy" CANADIAN JOURNAL OF CHEMISTRY, 82(2), 195-205 CODEN: CJCHAG; ISSN: 0008-4042, 2004, XP002395986 page 199; compound 24				34		
X	EP 0 735 031 A1 (SHISEIDO CO., LTD., JAPAN) 2 October 1996 (1996-10-02) page 24, line 50				34		
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<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <span style="margin-left: 200px;"><input checked="" type="checkbox"/> See patent family annex.</span>							
* Special categories of cited documents : <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; padding: 5px;">               *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             </td> <td style="width: 50%; padding: 5px;">               *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.                *&amp;* document member of the same patent family             </td> </tr> </table>						*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
*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			Date of mailing of the international search report				
23 August 2006			08/09/2006				
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  Fanni, S				

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/GB2006/001358

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 CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; ORA, AKIO ET AL: "Electrically conductive siloxane-epoxy resin adhesives for semiconductor devices" XP002395990 retrieved from STN Database accession no. 1991:560871 crosslinking catalyst with RN = 136468-11-6 & JP 03 084078 A2 (TORAY INDUSTRIES, INC., JAPAN) 9 April 1991 (1991-04-09) -----	34
X	WO 01/26652 A (SMITHKLINE BEECHAM CORPORATION; MILLER, WILLIAM, H; NEWLANDER, KENNETH) 19 April 2001 (2001-04-19) page 31; example 14 -----	34
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X	JP 62 155267 A (SANKYO CO LTD) 10 July 1987 (1987-07-10) page 3; compound 6 -----	34
X	FR 1 479 207 A (PIERRE MARCEL THEIL) 5 May 1967 (1967-05-05) example 4 -----	34
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X	WO 2004/022535 A (YAMANOUCHI PHARMACEUTICAL CO., LTD; TORAY INDUSTRIES, INC; MORIHIRA, K) 18 March 2004 (2004-03-18) page 45; example 56 -----	34
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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/GB2006/001358

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 2006/060461 A (SCHERING CORPORATION; GILBERT, ERIC, J; MILLER, MICHAEL, W; SCOTT, JAC) 8 June 2006 (2006-06-08) page 241; example 570 -----	34
A	WO 2004/072051 A (VERNALIS CAMBRIDGE LTD [GB]; CANCER REC TECH LTD [GB]; INST OF CANCER) 26 August 2004 (2004-08-26) page 1, paragraph 1 claim 1 and 3, definition of R1 -----	1,47
E	WO 2006/051808 A (KYOWA HAKKO KOGYO CO., LTD; KITAMURA, YUSHI; KANDA, YUTAKA; NAKASHIMA,) 18 May 2006 (2006-05-18) the whole document -----	1,47

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box II.1

Although claims 48-55 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.

## Continuation of Box II.1

Claims Nos.: 3, 48-55

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

## Continuation of Box II.2

Claims Nos.: 3

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty vis-à-vis present claim 3. Despite the use of 21 provisos, the subject matter of said claim still encompasses several known derivatives as simple as e.g. 4-hydroxy-benzoic acid alkyl amide derivatives. As a result, so many documents were retrieved that it is impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT).

For these reasons, the search was performed taking into consideration the non-compliance in determining the extent of the search of claim 3. Thus, the search has been restricted to the subject matter of use claims 1 and 2, i.e. the use of compounds of formula I and IO as inhibitors of Hsp90, and to compounds of formula V according to present claim 34.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB2006/001358

## 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.: 3, 48-55  
because they relate to subject matter not required to be searched by this Authority, namely:  
Although claims 48-55 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.: 3  
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:  
see FURTHER INFORMATION sheet PCT/ISA/210
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/GB2006/001358

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Information on patent family members

International application No

PCT/GB2006/001358

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