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(54) Title: BENZAZOLE DERIVATIVES, COMPOSITIONS, AND METHODS OF USE AS AURORA KINASE INHIBITORS

(57) Abstract: The present invention relates to compounds and methods from the treatment of cancer. The invention provides compounds that inhibit Aurora kinase, pharmaceutical compositions comprising compounds that inhibit Aurora kinase, and methods for the treatment of cancer using the compounds of the presentation invention or pharmaceutical compositions comprising compounds of the present invention.



WO 2007/095124 A3

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
 INV. C07D417/12 C07D403/12 A61K31/416 A61K31/4184 A61P35/00

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 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 practical, search terms used)
 EPO-Internal, CHEM ABS Data

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X	WO 03/082272 A (CHIRON CORP [US]; RENHOWE PAUL A [US]; RAMURTHY SAVITHRI [US]; AMIRI P) 9 October 2003 (2003-10-09) table 1, compounds 1-108; table 2, compounds 109-119; example 120; revendications 1-3, 6-86	1,2,4-6, 9,10,14, 16,32-40
X	US 6 303 600 B1 (COX PAUL JOSEPH [GB] ET AL) 16 October 2001 (2001-10-16) column 31, lines 42-46; columns 77-79; claims 1, 28, 30	1,2, 4-10,14, 16,32-40
X	US 6 114 532 A (RIES UWE [DE] ET AL) 5 September 2000 (2000-09-05) page 14, column 25, lines 32-33; examples; claim 1	1,2,4-6, 9,14,16, 32-40
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Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents :

<p>*A* document defining the general state of the art which is not considered to be of particular relevance</p> <p>*E* earlier document but published on or after the international filing date</p> <p>*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)</p> <p>*O* document referring to an oral disclosure, use, exhibition or other means</p> <p>*P* document published prior to the international filing date but later than the priority date claimed</p>	<p>*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</p> <p>*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</p> <p>*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.</p> <p>*Z* document member of the same patent family</p>
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Date of the actual completion of the international search 22 August 2007	Date of mailing of the international search report 04/09/2007
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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 Rufet, Jacques
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International application No

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X	WO 97/03069 A (GLAXO GROUP LTD [GB]; COCKERILL GEORGE STUART [GB]; CARTER MALCOLM CLI) 30 January 1997 (1997-01-30) claims 1,9,10,16,17; examples 1,3,4	1,2,4-6, 9,10,14, 16,32-40
X	WO 2005/016914 A (SMITHKLINE BEECHAM CORP [US]; RENO MICHAEL JOHN [US]; STEVENS KIRK LAW) 24 February 2005 (2005-02-24) page 1, line 30 - page 2, line 17; claims 1,21-27; examples 1-4,60	1,2,4-6, 14,16, 32-40
X	EP 0 260 744 A2 (JANSSEN PHARMACEUTICA NV [BE]) 23 March 1988 (1988-03-23) page 16, lines 30-32; compounds 40, 43, 69-71, 177; claims	1,2,4-6, 14,16, 32-40
X	WO 2004/063169 A (FUJISAWA PHARMACEUTICAL CO [JP]; URANO YASUHARU [JP]; SATOH SHIGEKI [J]) 29 July 2004 (2004-07-29) claims 1,17-20; table 2	1,2,9, 10,14, 16,32-40
P,X	WO 2006/086539 A (SMITHKLINE BEECHAM CORP [US]; JUNG DAVID KENDALL [US]; ALBERTI MICHAEL) 17 August 2006 (2006-08-17) claims 1,5-8,10; example 7	1,2,9, 10,14, 16,32-40
X	WO 98/02438 A (GLAXO GROUP LTD [GB]; COCKERILL GEORGE STUART [GB]; CARTER MALCOLM CLI) 22 January 1998 (1998-01-22) claims 1,24-30; examples 1-4	1,2,4, 10,14, 32-40
X	WO 96/39390 A (AMERICAN HOME PROD [US]) 12 December 1996 (1996-12-12) claims 1-6,10	1,2,4-6, 9,10,14, 16
X	EP 0 266 326 A1 (HAESSLE AB [SE]) 4 May 1988 (1988-05-04) page 4, line 15; claim 1; table 1	1,2,4-6, 9,10, 14-17, 32,33
X	US 6 316 474 B1 (MCCAULEY JOHN A [US] ET AL) 13 November 2001 (2001-11-13) claim 6	1,2,4-6
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International application No

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X	US 4 925 853 A (SMITH STEPHEN A [GB] ET AL) 15 May 1990 (1990-05-15) example 1, starting compound -----	1,2,4-6, 14-17, 32,33
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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.
X	DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; KUBO, KEIJI ET AL: "Benzimidazole derivatives as neovascularization inhibitors and pharmaceutical compositions containing them" XP002439668 retrieved from STN Database accession no. 2000:356164 abstract & JP 2000 143635 A (TAKEDA CHEMICAL INDUSTRIES, LTD., JAPAN) 26 May 2000 (2000-05-26)	1,2, 4-10,14, 16
P,X	WO 2006/099379 A (TRANSTECH PHARMA INC [US]; MJALLI ADNAN M M [US]; JONES DAVID [US]; GO) 21 September 2006 (2006-09-21) table 1, compounds 47-53,55; claims 1, 32, 39-41	1-7,9, 10,14, 17,32,33
X	WO 2004/085425 A1 (AMGEN INC., USA) 7 October 2004 (2004-10-07) claims 1-67; examples 1,2,11-14,16,19,21-25,50; table 5	1-6,9, 10, 12-17, 32-40
X	WO 2005/042520 A (MERCK PATENT GMBH [DE]; STAEHLE WOLFGANG [DE]; BUCHSTALLER HANS-PETER) 12 May 2005 (2005-05-12) page 76 - page 78; claims 1-36	1-7,10, 32-40
Y	claims 1,33-36	1-7,9, 10, 12-17, 20-24, 26-29, 32-40
Y	WO 03/053939 A (SOD CONSEILS RECH APPLIC [FR]; POITOUT LYDIE [FR]; BRAULT VALERIE [FR]) 3 July 2003 (2003-07-03) page 26 - page 27; claims 1-3,6,17	1-7,9, 10, 12-17, 20-24, 26-29, 32-40
X	WO 2004/087153 A2 (CHIRON CORPORATION, USA) 14 October 2004 (2004-10-14) abstract; claims 21,30; examples 1-4,7-10	1-6, 32-40
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/003579

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/032548 A (CHIRON CORP [US]; AMIRI PAYMAN [US]; FANTL WENDY [US]; LEVINE BARRY HA) 14 April 2005 (2005-04-14) claims 1-3,5-32,34-46,58-60,71-86; examples 1-99; table 1 -----	1-6, 32-40
X	EP 0 385 850 A2 (LABORATOIRES U.P.S.A., FR.) 5 September 1990 (1990-09-05) claim 17 -----	1-4,6, 32,33
X	DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; DAS, JAGABANDHU ET AL: "Preparation of cyclic protein tyrosine kinase inhibitors" XP002447592 retrieved from STN Database accession no. 2000:756524 RN:302963-85-5 abstract & WO 00/62778 A1 (BRISTOL-MYERS SQUIBB CO., USA) 26 October 2000 (2000-10-26) -----	1-3, 32-40
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/003579

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.: 35-40
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 35-40 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:

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 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.:
1,2,4-17,32-40 all partially and 3, 18-31 all complete
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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1,2,4-17,32-40 all partially

Provision of benzazole derivatives according to formula (I) wherein X is -NH- and E is -CH2- useful in treating cell proliferative disorders

2. claims: 1,2,4-17,32-40 all partially and 3, 18-31 all complete

Provision of benzazole derivatives according to formula (I) wherein X is -NH- and E is -NH- useful in treating cell proliferative disorders

3. claims: 1,2,4-17,32-40 all partially

Provision of benzazole derivatives according to formula (I) wherein X is -NH- and E is -O- useful in treating cell proliferative disorders

4. claims: 1,2,4-17,32-40 all partially

Provision of benzazole derivatives according to formula (I) wherein X is -NH- and E is -S- useful in treating cell proliferative disorders

5. claims: 1,2,4-17,32-40 all partially

Provision of benzazole derivatives according to formula (I) wherein X is -O- and E is -CH2- useful in treating cell proliferative disorders

6. claims: 1,2,4-17,32-40 all partially

Provision of benzazole derivatives according to formula (I) wherein X is -O- and E is -NH- useful in treating cell proliferative disorders

7. claims: 1,2,4-17,32-40 all partially

Provision of benzazole derivatives according to formula (I) wherein X is -O- and E is -O- useful in treating cell proliferative disorders

8. claims: 1,2,4-17,32-40 all partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Provision of benzazole derivatives according to formula (I)
wherein X is -O- and E is -S- useful in treating cell
proliferative disorders

9. claims: 1,2,4-17,32-40 all partially

Provision of benzazole derivatives according to formula (I)
wherein X is -S- and E is -CH2- useful in treating cell
proliferative disorders

10. claims: 1,2,4-17,32-40 all partially

Provision of benzazole derivatives according to formula (I)
wherein X is -S- and E is -NH- useful in treating cell
proliferative disorders

11. claims: 1,2,4-17,32-40 all partially

Provision of benzazole derivatives according to formula (I)
wherein X is -S- and E is -O- useful in treating cell
proliferative disorders

12. claims: 1,2,4-17,32-40

Provision of benzazole derivatives according to formula (I)
wherein X is -S- and E is -S- useful in treating cell
proliferative disorders

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2007/003579

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