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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: INHIBITORS OF AKT ACTIVITY

(57) Abstract: The present invention is directed to compounds which contain substituted naphthyridines which inhibit the activity of Akt, a serine/threonine protein kinase. The invention is further directed to chemotherapeutic compositions containing the compounds of this invention and methods for treating cancer comprising administration of the compounds of the invention. These substituted naphthyridines have unexpected advantageous properties when compared to other naphthyridines reported in PCT publication WO2003/086394, such unexpected advantageous properties may include increased cellular potency/solubility, greater selectivity, enhanced pharmacokinetic properties, lack of off target activity and so on.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/44294

A. CLASSIFICATION OF SUBJECT MATTER

IPC: A61K 31/4375(2006.01);A61K 31/4985(2006.01);C07D 401/14(2006.01),403/14(2006.01)

USPC: 546/123;544/365;514/303,252.12

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)

U.S. : 546/123; 544/365; 514/303,252.12

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)

CAS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US2004/0,102,360 (Barnett et al.) 27 May 2004 (27.5.2004), Claim 52 and pages 76-82	1-9
X	WO03084473 A2 (Barnett et al.) 16 October 2003 (16.10.2003), Example 22, pages 128-143	1-9
X	WO03086394 (Bilodeau et al.) 23 October 2003 (23.10.2003), Claim 2	1-9
A,P	Zhao et al., Discovery of 2,3,5-trisubstituted pyridine derivatives as potent Akt1 and Akt2 dual inhibitors, Bioorganic & Medicinal Chemistry Letters, 2005, Vol. 15, pages 905-909.	1-9

☐ 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 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

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/44294

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:
Please See Continuation 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 additional fees, this Authority did not invite payment of any 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.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/44294

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains different groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

PCT Rule 13.1 states that the international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention").

PCT Rule 13.2 states that the unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features.

Annex B, Part 1(a) indicates that the application should relate to only one invention. If there is more than one invention, inclusion is permitted if they are so linked to form a single general inventive concept.

Annex B Part 1(b) indicates that "special technical features" mean those technical features that as a whole define a contribution over the prior art.

Annex B Part 1(c) further defines independent and dependent claims. Unity of invention only is concerned in relation to independent claims. Dependent claims are defined as a claim that contain all the features of another claim and is in the same category as the other claim. The category of a claim refers to the classification of claims according to subject matter e.g. product, process, use, apparatus, means, etc.

Annex B Part 1(e) indicates the permissible combinations of different categories of claims. **Part 1(e)I** states that inclusion of an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for a use of the said product is permissible.

Annex B, Part 1(f) indicates the "Markush practice" of alternatives in a single claim. **Part 1(f)I** indicates the technical relationship and the same or corresponding special technical feature is considered to be met when (A) all alternatives have a common property or activity, and (B) a common structure is present or all alternatives belong to a recognized class of chemical compounds. Further defining (B), **Annex B, Part 1(f)(I-iii)m**, the common structure must: a) occupy a large portion of their structure, or b) the common structure constitutes a structurally distinctive portion, or c) where the structures are equivalent and therefore a recognized class of chemical compounds, each member could be substituted for one another with the same intended result. That is, with a common or equivalent structure, there is an expectation relationship and the corresponding special technical feature results from a common (or equivalent) structure that is responsible for the common activity (or property). **Part 1(f)iv** indicates that when all alternatives of a Markush grouping can be differently classified, it shall not, taken alone, be considered justification for finding a lack of unity. **Part 1(f)V** indicates that "When dealing with alternatives, if it can be shown that at least one Markush alternative is not novel over the prior art, the question of unity of invention shall be reconsidered by the examiner."

Group I, claim(s) 1-8, drawn to compounds and compositions wherein the saturated ring contains one nitrogen.

Group II, claim(s) 1-8, drawn to compounds and compositions wherein the saturated ring contains two nitrogen.

Group III, claim(s) 9, drawn to methods of use of a compound of claims 1-8.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The compounds lack an inventive step under PCT Article 33(3).