Title: TREATMENT OF CANCER USING BENZOIC ACID DERIVATIVES

Abstract: The present invention provides a method of treating cancer using benzoic acid derivatives, alone or in combination with standard treatments such as chemotherapy and radiotherapy. Also provided are methods of screening for benzoic derivatives based on their ability to inhibit the enzyme tyrosinase or to bind to and activate PXR/SXR xenobiotic receptors.
# INTERNATIONAL SEARCH REPORT

**International application No.**

PCT/US05/02402

## A. CLASSIFICATION OF SUBJECT MATTER

**IPC(7):** A61K 31/19, 31/235; C07C 63/06, 69/76  
**US CL:** 514/532, 568; 560/8; 562/405  
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.:** 514/532, 568; 560/8; 562/405

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)  
Please see Continuation Sheet

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y</td>
<td></td>
<td>1-4, 6-13</td>
</tr>
<tr>
<td>X</td>
<td>US 5,773,460 (GABOURY et al.) COL. 13-14, claims 1 and 8.</td>
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<td>X</td>
<td>US 5,958,980 (RHODES) 28 September 1999, see col. 14, claims 1-5.</td>
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<td>X</td>
<td>US 6,395,720 (KREUTZ) see col. 2 lines 15-col. 3 line 28, col. 8, claims 1-2.</td>
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</tbody>
</table>

- 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  

**Date of the actual completion of the international search:** 07 November 2005 (07.11.2005)  
**Date of mailing of the international search report:** 30 Nov 2005

**Name and mailing address of the ISA/US**  
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**Authorized officer:**  
Celia Chang  
Telephone No. 571-272-1600

Form PCT/ISA/210 (second sheet) (April 2005)
<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tbody>
<tr>
<td>X</td>
<td>US 6,740,777 (TSUKAMOTO et al.) see col. 68-70, compounds and claim 11 treating cancer.</td>
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<td>1-3, 6-13</td>
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<tr>
<td>X</td>
<td>US 6,825,233 (ERICSSON et al.) see whole article, especially, compounds and composition of claims 1-7, col. 39-42, and antitumor at col. 1 line 16.</td>
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<td>1-3, 6-13</td>
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<tr>
<td>A</td>
<td>Database CASPLUS on STN (Columbus, OH, USA) No. 93:114154 'amino-substituted phenyl and heteroaryl compounds and pharmaceutical compositions containing them' abstract, Shepherd, see RN 53624-18-3.</td>
<td>1-13</td>
</tr>
</tbody>
</table>
**INTERNATIONAL SEARCH REPORT**

**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.: 1-13

**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.

Form PCT/ISA/210  (continuation of first sheet(2)) (April 2005)
BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-13, drawn to method of treating cancer with compounds.

Group II, claims 14-15, drawn to screening method of receptor binding material.

Group III, claims 16-24, drawn to method of treating cancer using combination of compounds and radiation.

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:

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, or 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" means 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 contains 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 that the permissible combinations of different categories of claims. Part 1(e)(f), 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)(ii), 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 result 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 no, take 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."

In the instant case, at least one Markush alternative is not novel because prior art by Thomas et al. CA 110-4185 anticipated group II invention, thus the lacking of unity of invention has been found.

Continuation of B. FIELDS SEARCHED Item 3:
CAS--structure
East/West--image