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3 January 2013

(15) Information about Correction:

[Continued on next page]

(54) Title: SMALL MOLECULE MODULATORS OF SIRT1 ACTIVITY ACTIVATE P53 AND SUPPRESS TUMOR GROWTH



FIG.1C

(57) Abstract: Although ~50 % of all types of human cancers harbor wild type TP 53, this p53 tumor suppressor is often deactivated through a concerted action by its abnormally elevated suppressors, MDM2, MDMX, or SIRT1. Reported herein are small molecules such as Inauhzin that effectively reactivates p53 by inhibiting SIRT1 activity, promotes p53 -dependent apoptosis of human cancer cells without causing apparently genotoxic stress. Moreover, Inauhzin stabilizes p53 by increasing p53 acetylation and preventing MDM2 -mediated ubiquitylation of p53 in cells, though not directly in vitro. Remarkably, Inauhzin inhibits cell proliferation, induces senescence and tumor-specific apoptosis, and represses the growth of xenograft tumors derived from p53- harboring H460 and HCT116 cells without causing apparent toxicity to normal tissues and the tumor-bearing SCID mice. As reported herein, Inauhzin is an anti-cancer therapeutic candidate that inhibits SIRT1 activity and activates p53.



**Previous Correction:**  
see Notice of 22 November 2012

## INTERNATIONAL SEARCH REPORT

International application No.  
**PCT/US2012/030619****A. CLASSIFICATION OF SUBJECT MATTER*****A61K 31/53(2006.01)i, A61K 31/5415(2006.01)i, A61P 35/00(2006.01)i***

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)

A61K 31/53; C12N 5/02; A61K 31/4985; C12P 19/00; A61K 48/00; C12P 7/64

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

eKOMPASS(KIPO internal), Google &amp; PubMed

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	WO 2010-111711 A2 (ZACHARON PHARMACEUTICALS, INC.) 30 September 2010 See claims 1, 13-15; figure 36C.	6 10
A	US 2010-0035885 A1 (SINCLAIR, D. A. et al.) 11 February 2010 See abstract; claims 40, 45.	6, 10
A	WO 2008-106507 A2 (UNIVERSITY OF SOUTH FLORIDA) 04 September 2008 See claims 1, 2; p. 1, lines 10-11; p. 3, lines 23-24.	6, 10
PX	ZHANG, Q. et al., 'A small molecule Inauhzin inhibits SIRT1 activity and suppresses tumour growth through activation of p53', EMBO Mol. Med., Epub 13 Feb. 2012, Vol. 4, No. 4, pp. 298-312 See abstract; p. 306, right column, line 1-p.307 left column line 13; p.310 left column line 22-right column line 9; figure 1.	6, 10

 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 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 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

"&amp;" document member of the same patent family

Date of the actual completion of the international search

20 SEPTEMBER 2012 (20.09.2012)

Date of mailing of the international search report

**04 OCTOBER 2012 (04.10.2012)**

Name and mailing address of the ISA/KR

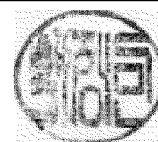
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**INTERNATIONAL SEARCH REPORT**

International application No.

**PCT/US2012/030619****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.: 1-5, 7-9, 11-23  
because they relate to subject matter not required to be searched by this Authority, namely:  
Claims 1-5, 7-9, 11-23 pertain to methods of treatment of the human body by therapy, and thus relate to a subject matter which this International Searching Authority is not required to search under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT.
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:

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 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**

Information on patent family members

International application No.

**PCT/US2012/030619**

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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