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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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(54) Title: COMPOSITIONS AND METHODS FOR EFFECTING NAD⁺ LEVELS USING A NICOTINAMIDE PHOSPHORIBOSYL TRANSFERASE INHIBITOR

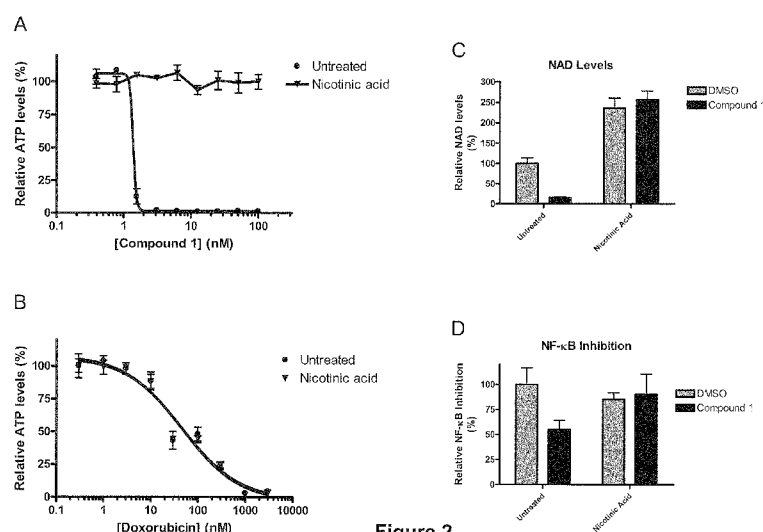


Figure 2

(57) Abstract: The present invention relates to methods for decreasing cellular DNA repair in a target patient; decreasing cellular NAD⁺ biosynthesis in a target patient; increasing efficiency of radiation therapy in a target patient; modulating nicotinamide phosphoribosyl transferase activity in a patient; or sensitizing a patient to a DNA damaging therapy. The invention relates to methods for treating a patient who received a toxic dose of an nicotinamide phosphoribosyl transferase inhibitor. The invention also relates to pharmaceutical compositions comprising a physiologically acceptable carrier; an effective amount of a NMPRT inhibitor; and nicotinic acid. The invention also relates to methods for treating a patient diagnosed with or suspected to have a cancer deficient in nicotinic acid pathway.

INTERNATIONAL SEARCH REPORT

International application No.
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A. CLASSIFICATION OF SUBJECT MATTER

IPC: **A61K 31/455** (2006.01) , **A61K 31/44** (2006.01) , **A61K 31/4409** (2006.01) , **A61K 31/4425** (2006.01) , **A61P 35/00** (2006.01) and **A61P 39/00** (2006.01)

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 31/455 (2006.01) , **A61K 31/44** (2006.01) , **A61K 31/4409** (2006.01) , **A61K 31/4425** (2006.01) , **A61P 35/00** (2006.01) and **A61P 39/00** (2006.01)

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

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

Databases: STN CAPLUS, Internet: NCBI, PubMed, Medline, Google Scholar, Canadian Patent Database, QPat, Delphion, Espacenet, Patentscope. Keywords used: nicotinamide, phosphoribosyltransferase, NMPRT, NAPRT, CHS 828, FK866, nicotinic acid, CAS RN 59-67-6, niacin, cancer, DNA, damaging, repair, NAD, biosynthesis, modulating, sensitizing and toxic.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	OLESEN ET AL., "Anticancer Agent CHS-828 Inhibits Cellular Synthesis of NAD", <i>Biochemical and Biophysical Research Communications</i> , 367 (15 January 2008 (15-01-2008)) 799-804. Full Document	1 to 54
X	US 5696140 (BRAMM ET AL.) 9 December 1997 (09-12-1997) See in particular example 43 and claims 1 and 7 whole document	26 to 37
X	US 6525077 (BINDERUP ET AL.) 25 February 2003 (25-02-2003) See in particular, example 9 and claims 1, 2, 17, 23 and 24 whole document	26 to 37

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"&" document member of the same patent family
"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

7 July 2009 (07-07-2009)

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Marie C. Letellier 819- 997-2941

INTERNATIONAL SEARCH REPORTInternational application No.
PCT/IB2008/003828**Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the 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. ☒ Claim Nos. : Claims 1 to 51

because they relate to subject matter not required to be searched by this Authority, namely :

Claims 1 to 51 are directed to a method for treatment of the human or animal body by surgery or therapy which the International Search Authority is not required to search. However, this Authority has carried out a search based on the alleged effects or purposes/uses of the product defined in claims 1 to 51.

2. ☐ Claim 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. ☐ Claim 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 :

See the Extra 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 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 claim 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 claim 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/IB2008/003828

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5919816 (HAUSHEER ET AL.) 6 July 1999 (06-07-1999) whole document	1 to 25 and 38 to 54
A	HASMANN ET AL., "FK866, a Highly Specific Noncompetitive Inhibitor of Nicotinamide Phosphoribosyltransferase, Represents a Novel Mechanism for Induction of Tumor Cell Apoptosis", <i>Cancer Research</i> , 63 (1 November 2003 (01-11-2003)) 7436-7442. Full Document	1 to 54

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2008/003828

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
US 5696140A	09-12-1997	AT 141262T	15-08-1996
		AU 670816B2	01-08-1996
		AU 4945693A	12-04-1994
		CA 2143756A1	31-03-1994
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2008/003828

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
US 5919816A	06-07-1999	AT 237337T	15-05-2003
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INTERNATIONAL SEARCH REPORT

International application No.
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The common linking feature of the subject matter of claims 1-51 is the use of a nicotinamide phosphoribosyl transferase inhibitor for the treatment of cancer. However, this linking feature is not novel (see *Cancer Research*, 63, November 2003, 436-7442, US 5696140 and US 6525077) and cannot represent the single inventive concept which could have linked the different claimed subject matter together. Therefore, the claims are directed to a plurality of alleged inventions as follows:

Group A - Claims 1-10 and 47-54 are directed to a composition containing a nicotinamide phosphoribosyl transferase inhibitor and nicotinic acid as well as the use of said composition for the treatment of cancer deficient in nicotinic acid pathway,

Group B - Claims 26-37 are directed to the use of a nicotinamide phosphoribosyl transferase inhibitor for the treatment of cancer deficient in nicotinic acid pathway, and

Group C - Claims 38-46 are directed to the combination therapy of a nicotinamide phosphoribosyl transferase inhibitor and a DNA damaging therapy for the treatment of cancer deficient in nicotinic acid pathway.

Claims 11-25 can go either with **Group A** or **C**.