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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, CL, 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, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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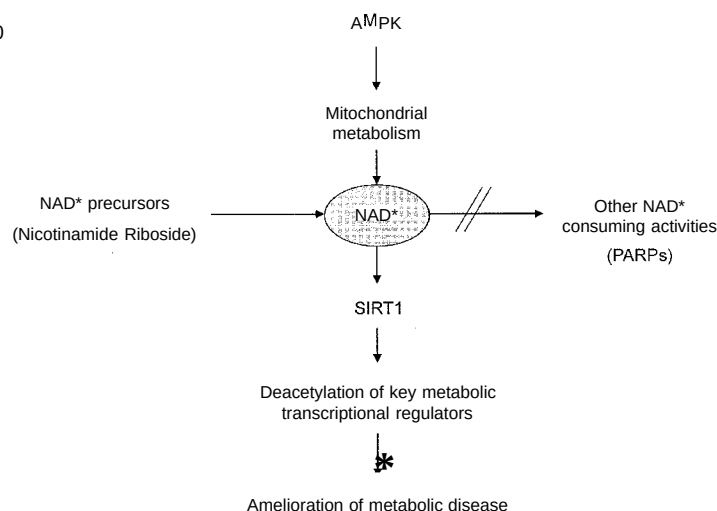
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[Continued on next page]

(54) Title: METHODS OF TREATING MITOCHONDRIAL DYSFUNCTION

Figure 40



(57) **Abstract:** The present invention provides methods of treating various disorders associated with mitochondrial dysfunction, including but not limited to metabolic disorders, neurodegenerative diseases, chronic inflammatory diseases, and diseases of aging.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2012/001146

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/05 A61K31/405 A61K31/502 A61K31/7064
ADD.

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

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)

EPO-Internal , WPI Data, BIOSIS, CHEM ABS Data, COMPENDEX, EMBASE, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	wo 2009/089011 A2 (SI RTRI S PHARMACEUTICALS INC [US] ; LUNSMANN WALTER JOSEPH [US] ; ELLIOTT) 16 July 2009 (2009-07-16) page 9, line 25 - page 10, line 3 page 16, line 10 - line 19 page 17, line 12 - line 14 -----	1-4,6,7 , 9, 10
X	US 2007/244202 A1 (MURASE TAKATOSHI [JP]) 18 October 2007 (2007-10-18) paragraphs [0014] , [0019] -----	1-4,6,7 , 9, 10
X	wo 2009/054994 A2 (HARVARD COLLEGE [US] ; SINCLAIR DAVID A [US] ; CARMONA JUAN [US]) 30 April 2009 (2009-04-30) page 12, line 17 - line 25 page 15, line 17 - line 22 ----- -/-- -	1-4,6,7 , 9, 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

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"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

31 January 2013

Date of mailing of the international search report

12/04/2013

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

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PCT/IB2012/001146

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 2009/080033 AI (FERTIN PHARMA AS [DK] ; BRUUN HEIDI ZIEGLER [DK] ; ANDERSEN CARSTEN [DK]) 2 July 2009 (2009-07-02) abstract -----	1-4,6,7 , 9, 10
X	wo 2009/140265 A2 (CHILDRENS MEDICAL CENTER [US] ; OZCAN UMUT [US] ; OZCAN LALE [US]) 19 November 2009 (2009-11-19) abstract -----	1-4,6,7 , 9, 10
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X	wo 01/93874 AI (UNIV BRIGHAM YOUNG [US] ; WINDER WILLIAM [US]) 13 December 2001 (2001-12-13) abstract -----	1-4,6,7 , 9, 10
X	wo 2009/019600 A2 (REDDYS LAB LTD DR [IN] ; MISRA PARIMAL [IN] ; CHAKRABARTI RANJAN [IN] ; M) 12 February 2009 (2009-02-12) abstract -----	1-4,6,7 , 9, 10
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2012/001146

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:

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 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 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. :

1-4, 6-10(al l parti al ly)

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.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-4, 6-10 (all partially)

a method of treating obesity by administering a compound that increases intracellular nicotinamide adenine dinucleotide (NAD⁺) in an amount sufficient to activate SIRT1 or SIRT3.

2. claims: 1-4, 6-10 (all partially)

a method of treating type II diabetes by administering a compound that increases intracellular nicotinamide adenine dinucleotide (NAD⁺) in an amount sufficient to activate SIRT1 or SIRT3.

3. claims: 1-4, 6-10 (all partially)

a method of treating a neurodegenerative disease by administering a compound that increases intracellular nicotinamide adenine dinucleotide (NAD⁺) in an amount sufficient to activate SIRT1 or SIRT3.

4. claims: 1-4, 6-10 (all partially)

a method of treating an aging related disorder by administering a compound that increases intracellular nicotinamide adenine dinucleotide (NAD⁺) in an amount sufficient to activate SIRT1 or SIRT3.

5. claims: 1-4, 6-10 (all partially)

a method of treating a chronic inflammatory disease by administering a compound that increases intracellular nicotinamide adenine dinucleotide (NAD⁺) in an amount sufficient to activate SIRT1 or SIRT3.

6. claims: 5, 7-10 (all partially)

a method of treating cancer by administering a PARP inhibitor and a NAD⁺ booster.

7. claims: 5, 7-10 (all partially)

a method of treating cancer by administering a PARP inhibitor and an AMPK agonist.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

8. claims : 5, 7-10(al l parti al ly)

a method of treati ng cancer by admini steri ng an AMPK agoni st
and a NAD+ i nhi bi tor.

9. claims : 11-13

a method of increasi ng the concentrati on of NAD+/acti vati ng
mi tochondri al si rtui n by contacti ng mi tochondri a wi th
ni coti nami de ri boside

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2012/001146

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Information on patent family members

International application No

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