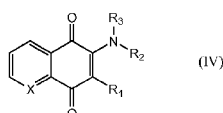




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- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, 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, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, 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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[Continued on next page]

(54) Title: INHIBITORS OF THE MITF MOLECULAR PATHWAY



(57) Abstract: Provided herein are compounds of the formula (IV) as well as pharmaceutically acceptable salts thereof, wherein the substituents are as those disclosed in the specification. These compounds, and the pharmaceutical compositions containing them, are useful as MITF inhibitors, MITF pathway inhibitors and for the treatment of cancer.

Effect of ML329 on MITF and MITF-dependent gene expression in primary melanocytes

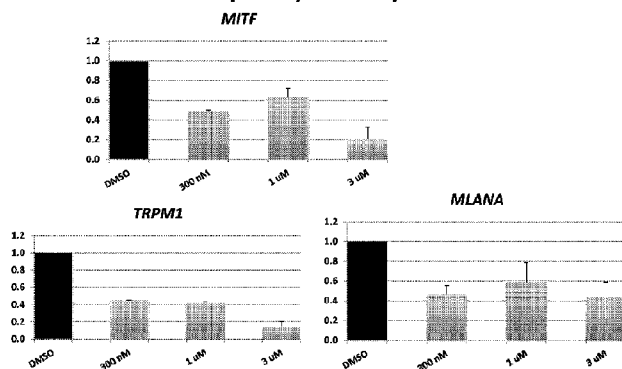


FIG. II



TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

Published:

— *with international search report (Art. 21(3))*

(88) Date of publication of the international search report:
5 February 2015

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/41730

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.: 11, 13, 15 and 17
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:
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 1-10 and 12 directed to bicyclic quinone derivatives of Formula (IV), represented by Formula (I), Formula (Ia), Formula (Ib), Formula (Ic), Formula (Id) and Formula (III). Group I+ will be searched to the extent that it reads on a bicyclic quinone derivative of Formula (IV), represented by the compound specified in claim 12. It is believed that claims 1-5 and 12 read on this first-named invention. Applicants must indicate, if applicable, the claims which read on the first named invention if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. An exemplary election would be a compound of formula (IV) represented by Formula (III) (i.e. claims 1, 3-5 and 10).

-Please see continuation in attached 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 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.:
1-5 and 12

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/US 14/41730

A. CLASSIFICATION OF SUBJECT MATTER IPC(8) - A61K 31/12; A61K 31/135 (2014.01) CPC - A01N 33/18; C07C 225/22; A61K 31/12; C07C 49/747 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) IPC(8): A61K 31/12; A61K 31/135 (2014.01) CPC: A01N 33/18; C07C 225/22; A61K 31/12; C07C 49/747 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched USPC: 514/680; 514/658 Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PatBase, Google Scholar, SureChem, PubWEST naphthoquinone, 1,4-dioxo-1,2-dihydronaphthalen-2-yl, benzenesulfonamide, cancer, 4-((1,4-dioxo-1,4-dihydro naphthalen-2-yl)amino) benzenesulfonamide										
C. DOCUMENTS CONSIDERED TO BE RELEVANT										
<table border="1"> <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>X</td> <td>US 2011/0201609 A1 (LAWRENCE et al.) 18 August 2011 (18.08.2011) para [0027], [0032]</td> <td>1-5</td> </tr> <tr> <td>X</td> <td>PUBCHEM CID 12387471 (Create Date: 08 February 2007) pg 1, Fig; pg 2, Table</td> <td>1-2, 12</td> </tr> </tbody> </table>	Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	X	US 2011/0201609 A1 (LAWRENCE et al.) 18 August 2011 (18.08.2011) para [0027], [0032]	1-5	X	PUBCHEM CID 12387471 (Create Date: 08 February 2007) pg 1, Fig; pg 2, Table	1-2, 12	
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X	PUBCHEM CID 12387471 (Create Date: 08 February 2007) pg 1, Fig; pg 2, Table	1-2, 12								
<input type="checkbox"/> Further documents are listed in the continuation of Box C.										
* 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 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 10 November 2014 (10.11.2014)	Date of mailing of the international search report 10 DEC 2014									
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774									

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/41730

Attachment to Box.No.III: -continued-

Group II: Claims 14 and 16 directed to a pharmaceutical composition containing a therapeutically effective amount of a compound of formula (II), or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier and to method for treating cancer, comprising administering a therapeutically effective amount of said compound or salt to a subject in need thereof.

The inventions listed as Group I+ and II 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:

Special technical features:

Each invention of Group I+ is a unique chemical compound and is not shared by any other invention of Group I+.

Group II includes the technical feature of a compound of Formula II, a composition containing the same and a method of treatment, not required by Group I+.

The compounds of Group I+ and II are structurally different compounds which do not share a common core structure.

Common technical features:

The inventions of Group I+ share the technical feature of a naphthoquinone compound of Formula (IV). This shared technical feature, however, does not provide a contribution over the prior art as being anticipated by PubChem CID 12387471 (Create Date- 08 February 2007) which discloses a compound of Formula (IV), wherein: X is CH; R1 and R3 are each hydrogen; R2 is a substituted aryl (pg 1, Fig). As said compound was known in the art at the time of the invention this cannot be considered a special technical feature that would otherwise unify the inventions of Group I+.

Groups I+ and II, thus lack unity under PCT Rule 13.2, because they do not share a same or corresponding special technical feature providing a contribution over the prior art.

Note reg. item 4: Claims 11, 13, 15 and 17 are unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). These claims are, therefore, not included in the above analysis.