The present invention is directed to compounds that are inhibitors of the deubiquitinating enzyme, USP14, encompassed by the Formulae (I), (Ia) and (lb), compositions thereof, methods for the treatment of a condition associated with a dysfunction in proteostasis, methods for enhancing proteasome activity and methods for treating conditions associated with proteostasis dysfunction, such as cancer or tumor.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

<table>
<thead>
<tr>
<th>IPC(8)</th>
<th>USPC</th>
</tr>
</thead>
<tbody>
<tr>
<td>A61K 31/519 (2013.01)</td>
<td>514/267; 514/260.1</td>
</tr>
</tbody>
</table>

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 31/519 (2013.01)

USPC: 514/267; 514/260.1 (text search)

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

USPC: 514/257; 544/249-250, 278 (text search) Find search terms below

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

PubMed (PGPB, USPTO, USOC, E PAB, JPA B), Google Scholar, WIPO, SureChem, PatentBase

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>X</td>
<td>US 2010/0227853 A1 (HOFFMAN et al.) 09 September 2010 (09.09.2010) para [0050]-[0063], [0073], [0075], [0079], [0083]</td>
<td>1-6, 18-20, 53-58 and 71-72</td>
</tr>
<tr>
<td>Y</td>
<td>WO 2004/065391 A1 (TERRICABRAS BELART et al.) 05 August 2004 (05.08.2004) pg 1, in 3-9, pg 74, In 1-2, Example 75, pg 84, In 21-22, Example 97</td>
<td>59 and 73-74</td>
</tr>
<tr>
<td>Y</td>
<td>CARD et al. A family of phosphodiesterase inhibitors discovered by cocrystallography and scaffold-based drug design, NATURE BIOTECHNOLOGY, February 2005, Vol.23, No.2, pp 201-207, [Retrieved from the internet on 10 March 2013 from the URL: <a href="http://journals.pasteur.jh.edu/">http://journals.pasteur.jh.edu/</a>] pg 202, col 1, para 2 - pg 206, col 1, para 2; Fig 1; Fig 3; Table 1</td>
<td>73-74</td>
</tr>
</tbody>
</table>

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
  - "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
  - "Z" document member of the same patent family

Date of the actual completion of the international search
09 March 2013 (09.03.2013)

Date of mailing of the international search report
27 MAR 2013

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. 703-306-3201

Authorized officer: Lee W. Young
PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-3774

Form PCT/ISA/210 (second sheet) (July 2009)
<table>
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<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
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</tr>
</thead>
</table>
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.: 7-17, 21-52, 65-70 and 75,92 because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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 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.:

**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.