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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

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(54) Title: COMPOSITIONS AND METHODS FOR MODULATION OF MCL-1 EXPRESSION

(57) Abstract: Disclosed herein are compounds, compositions and methods for modulating the expression of Mcl-1 in a cell, tissue or animal. Also provided are methods of target validation. Also provided are uses of disclosed compounds and compositions in the manufacture of a medicament for treatment of diseases and disorders.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/006706

A. CLASSIFICATION OF SUBJECT MATTER

INV. C12N15/11 A61K31/712 A61K31/7125 A61P35/00

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)

C12N A61K A61P

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 practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|---|-----------------------|
| X,L | WO 00/40595 A (ISIS PHARMACEUTICALS, INC. [US]) 13 July 2000 (2000-07-13) | 1,5-27 |
| Y | L: priority the whole document ISIS 20404 page 63; table 4 | 2 |
| X | MOULDING D.A. ET AL.: "Apoptosis is rapidly triggered by antisense depletion of MCL-1 in differentiating U937 cells" BLOOD, vol. 96, 2000, pages 1756-1763, XP002453593 | 1,5-27 |
| Y | the whole document page 1758; figure 2A | 2 |

 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 document 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

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28/12/2007

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Authorized officer

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2007/006706

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:

Although claims 20-22 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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 allsearchable 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.:

1-2, 5-27 all partially

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: 1-2, 5-27 all partially

An oligomeric compound related to SEQ ID NO:43, SEQ ID NO:44, or that hybridizes to the target region defined by nucleotides 123-150 of Mcl-1 as in SEQ ID NO:2.

2. claims: 1, 2, 5-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:45.

3. claims: 1, 2, 5-27 all partially

An oligomeric compound related to SEQ ID NO:46, 47, or that hybridizes to the target region defined by nucleotides 719-748 of Mcl-1 as in SEQ ID NO:2.

4. claims: 1-27 all partially

An oligomeric compound related to SEQ ID NO:48-65, SEQ ID NO:109-111, or that hybridizes to the target region defined by nucleotides 808-839, 902-930, 902-1007, 938-1007, 1039-1074, 1083-1150, 1104-1128 of Mcl-1 as in SEQ ID NO:2.

5. claims: 1, 2, 5-27 all partially

An oligomeric compound related to SEQ ID NO:66-72, or that hybridizes to the target region defined by nucleotides 1252-1297, 1396-1423 of Mcl-1 as in SEQ ID NO:2.

6. claims: 1, 2, 5-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:73.

7. claims: 1, 2, 5-27 all partially

An oligomeric compound related to SEQ ID NO:74-76, or that hybridizes to the target region defined by nucleotides 1651-1693 of Mcl-1 as in SEQ ID NO:2.

8. claims: 1, 2, 5-27 all partially

An oligomeric compound related to SEQ ID NO:77-80, or that hybridizes to the target region defined by nucleotides 1809-1851 of Mcl-1 as in SEQ ID NO:2.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

9. claims: 1, 2, 5-27 all partially

An oligomeric compound related to SEQ ID NO:81-83, or that hybridizes to the target region defined by nucleotides 2062-2103 of Mcl-1 as in SEQ ID NO:2.

10. claims: 1-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:84-88.

11. claims: 1, 2, 5-27 all partially

An oligomeric compound related to SEQ ID NO:89-91, or that hybridizes to the target region defined by nucleotides 2551-2585 of Mcl-1 as in SEQ ID NO:2.

12. claims: 1-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:92.

13. claims: 1, 2, 5-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:93, SEQ ID NO:94.

14. claims: 1-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:95.

15. claims: 1-27 all partially

An oligomeric compound related to SEQ ID NO:96-102, 112, or that hybridizes to the target region defined by nucleotides 3118-3161, 3176-3202, 3214-3254 of Mcl-1 as in SEQ ID NO:2.

16. claims: 1, 2, 5-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:103.

17. claims: 1, 2, 5-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:104.

18. claims: 1, 2, 5-13, 15-27 all partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

An oligomeric compound related to SEQ ID NO:105.

19. claims: 1, 2, 5-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:106.

20. claims: 1, 2, 5-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:107, SEQ ID NO:108.

21. claims: 1, 2, 5-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:113.

22. claims: 1, 2, 5-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:114.

23. claims: 1, 2, 5-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:115.

24. claims: 1, 2, 5-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:116.

25. claims: 1, 2, 5-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:117, 118.

26. claims: 1, 2, 5-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:119.

27. claims: 1, 2, 5-13, 15-27 all partially

An oligomeric compound related to SEQ ID NO:120.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2007/006706

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
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| WO 0040595 | A | 13-07-2000 | AU 2180700 A | 24-07-2000 |
| | | | EP 1140971 A1 | 10-10-2001 |
| | | | JP 3998089 B2 | 24-10-2007 |
| | | | JP 2002534073 T | 15-10-2002 |
| | | | US 6001992 A | 14-12-1999 |
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