

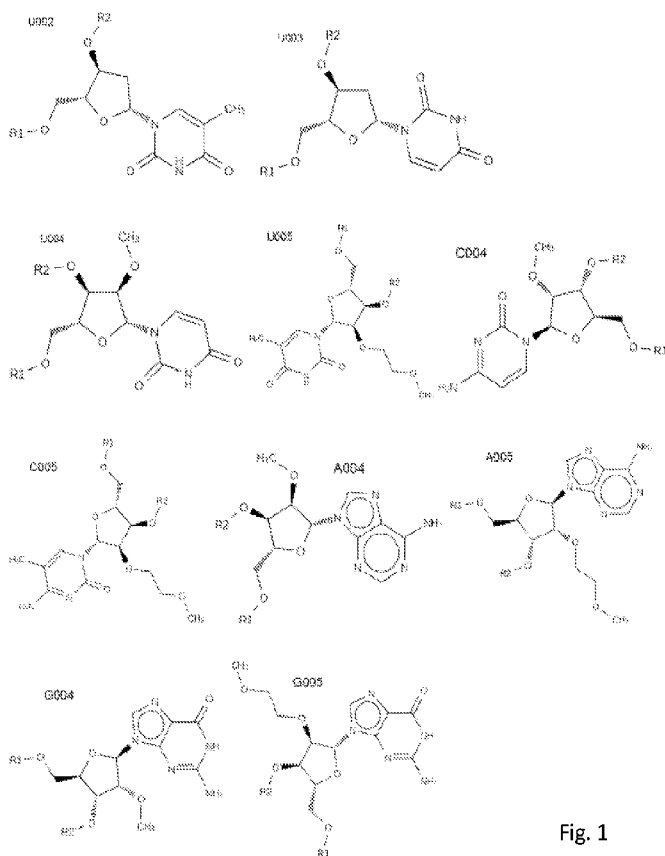


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[Continued on next page]

(54) Title: ORGANIC COMPOSITIONS TO TREAT KRAS-RELATED DISEASES



(57) Abstract: The present disclosure relates to RNAi agents useful in methods of treating KRAS-related diseases such as a proliferative disease, including without limitation a solid or liquid cancer, adenocarcinoma, colorectal cancer, advanced and/or metastatic colorectal cancer, colon cancer, lung, non-small cell lung cancer and lung adenocarcinoma, acute myelogenous lung, bladder, brain, breast, cervical, endometrial, gastric, head and neck, kidney, leukemia, myelodysplastic syndrome, myeloid leukemia, liver, melanoma, ovarian, pancreatic, prostate, testicular, thyroid cancers, and cardio-facio-cutaneous (CFC) syndrome and Noonan syndrome, and similar and related diseases, using a therapeutically effective amount of a RNAi agent to KRAS.

Fig. 1

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3 January 2014

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER  
INV. C12N15/113 A61P35/00  
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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

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, BIOSIS, MEDLINE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/108217 A2 (INTRADIGM CORP [US]; XIE FRANK Y [US]; YANG XIAODONG [US]; LIU YING [U] 3 September 2009 (2009-09-03) the whole document	1-22
X	WO 2010/115206 A2 (DICERNA PHARMACEUTICALS INC [US]; BROWN BOB D [US]) 7 October 2010 (2010-10-07) the whole document	1-22
X	WO 2010/115202 A2 (DICERNA PHARMACEUTICALS INC [US]; BROWN BOB D [US]) 7 October 2010 (2010-10-07) the whole document	1-22
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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

"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  23 July 2013	Date of mailing of the international search report  28/10/2013
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer  Spindler, Mark-Peter

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2013/038847

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 2008/109516 A2 (MDRNA INC [US]; QUAY STEVEN C [US]; MCSWIGGEN JAMES [US]; VAISH NAREND) 12 September 2008 (2008-09-12) the whole document -----	1-22
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A		9-18
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A		9-18
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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2013/038847

## 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.:

1-22(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: 1-22(partially)

composition comprising an RNAi agent targeting KRAS wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0-3 nucleotides from the sequence set forth in SEQ ID NO: 428 (optionally the sense strand of said RNAi agent comprises at least 15 contiguous differing by 0-3 nucleotides from the sequence set forth in SEQ ID NO: 1); medical implementations of said RNAi agent

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2-433. claims: 1-22(partially)

as in 1) but wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0-3 nucleotides from the sequence set forth in SEQ ID NO: 429-854, 1789-1791, 2763, 2765 or 2766, respectively (RNAi agents of tables 1, 1a and 1b having the same AD-identifier but different SEQ ID NOs were counted as one invention)

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## INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2013/038847

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2013/038847

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