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- (71) Applicant (for all designated States except US): DHARMA-  
MACON, INC. [US/US]; 2650 Crescent Drive, Suite 100,  
Lafayette, CO 80026 (US).
- (72) Inventors: LEAKE, Devin; 3050 S. Krameria St., Den-  
ver, CO 80222 (US). KHVOROVA, Anastasia; 4450  
Squires Circle, Boulder, CO 80305 (US). FEDOROV,  
Yuriy; 2405 Andrew Drive, Superior, CO 80027 (US).  
DELANEY, Michael, O.; 6300 Snowberry Avenue, Fire-  
stone, CO 805040 (US). ROBERTSON, Barbara; 455  
Hawthorn Ave, Boulder, CO 80304 (US). ANDERSON,  
Emily; Lafayette, CO 80026 (US).
- (74) Agents: KALOW, David et al.; Kalow & Springut, LLP,  
488 Madison Avenue, 19th floor, New York, NY 10022  
(US).
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ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: STABILIZED RNAS AS TRANSFECTION CONTROLS AND SILENCING REAGENTS

(57) Abstract: RNA molecules, including siRNA molecules and related control, trackability and exaequo agents with specific stability modifications are provided. These molecules are particularly advantageous as transfection control reagents. The molecules include first and second 5' terminal sense nucleotides with 2'-O-alkyl groups and a label on the first 5' terminal sense nucleotide, in conjunction with at least one additional 2'-O-alkyl pyrimidine modified sense nucleotide, and either: (i) at least one 2' fluoro modified pyrimidine antisense nucleotide and a phosphorylated first 5' terminal antisense nucleotide; or (ii) a first and second 5' terminal antisense nucleotide with 2'-O-alkyl modifications and at least one additional 2'-O-alkyl pyrimidine modified antisense nucleotide.

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INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2005/003365

A. CLASSIFICATION OF SUBJECT MATTER  
C12N15/11 A61K31/7088

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 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	HOLEN T. ET AL.: "Similar behaviour of single-strand and double-strand siRNAs suggests they act through a common RNAi pathway" NUCLEIC ACIDS RESEARCH, vol. 31, no. 9, 1 May 2003 (2003-05-01), pages 2401-2407, XP002283906 ISSN: 0305-1048 table 1 the whole document  ----- -/-	28,58, 62,63

Further documents are listed in the continuation of box C.

Patent family members are listed in 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.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

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Name and mailing address of the ISA  
European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Macchia, G

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2005/003365

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>HOLEN T. ET AL.: "Positional effects of short interfering RNAs targeting the human coagulation trigger Tissue Factor"            NUCLEIC ACIDS RESEARCH,            vol. 30, no. 8,            15 April 2002 (2002-04-15), pages            1757-1766, XP002232890            ISSN: 0305-1048            hTF167i            page 1759; figure 1</p>	
X	<p>AMARZGUIQUI M. ET AL.: "Tolerance for mutations and chemical modifications in a siRNA"            NUCLEIC ACIDS RESEARCH,            vol. 31, no. 2,            15 January 2003 (2003-01-15), pages            589-595, XP002281440            ISSN: 0305-1048            the whole document</p>	28,58
X	<p>CZAUDERNA F. ET AL.: "Structural variations and stabilising modifications of synthetic siRNAs in mammalian cells"            NUCLEIC ACIDS RESEARCH,            vol. 31, no. 11, 1 June 2003 (2003-06-01),            pages 2705-2716, XP002270732            ISSN: 0305-1048            figure 5            the whole document</p>	28,58, 62,63
A	<p>HARBORTH J. ET AL.: "Sequence, chemical, and structural variation of small interfering RNAs and short hairpin RNAs and the effect on mammalian gene silencing"            ANTISENSE &amp; NUCLEIC ACID DRUG DEVELOPMENT,            vol. 13, no. 2, April 2003 (2003-04),            pages 83-105, XP002284355            ISSN: 1087-2906            page 92, right-hand column            the whole document</p>	
A	<p>BRAASCH D.A. ET AL.: "RNA interference in mammalian cells by chemically-modified RNA"            BIOCHEMISTRY,            vol. 42, no. 26, 2003, pages 7967-7975,            XP002328494            ISSN: 0006-2960            figure 6            the whole document</p>	

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INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2005/003365

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>PARRISH S. ET AL.: "Functional anatomy of a dsRNA trigger: differential requirement for the two trigger strands in RNA interference" MOLECULAR CELL, vol. 6, no. 5, November 2000 (2000-11), pages 1077-1087, XP002226298 ISSN: 1097-2765 figure 5 the whole document</p>	
A	<p>NYKÄNEN A. ET AL.: "ATP requirements and small interfering RNA structure in the RNA interference pathway" CELL, vol. 107, 2 November 2001 (2001-11-02), pages 309-321, XP002969117 ISSN: 0092-8674 the whole document</p>	
A	<p>CHIU Y.-L. AND RANA T.M.: "siRNA function in RNAi: a chemical modification analysis" RNA, vol. 9, 2003, pages 1034-1048, XP002336178 the whole document</p>	

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2005/003365

## Box 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 26, 58 and 61 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 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 fee, this Authority did not invite payment of any additional fee.
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.:  
  
1-14, 26, 28, 55-58, 62, 63
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.
- 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: 1-14, 26, 55-57

An RNA duplex as claimed in the claims mentioned above, and methods related thereto.  
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2. claims: 15-25, 27

An RNA duplex as claimed in the claims mentioned above, and methods related thereto.  
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3. claims: 28, 58, 62, 63

An RNA duplex as claimed in the claims mentioned above, and methods related thereto.  
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4. claims: 29, 59

An RNA duplex as claimed in the claims mentioned above, and methods related thereto.  
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5. claims: 30, 60

An RNA duplex as claimed in the claims mentioned above, and methods related thereto.  
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6. claims: 31-38, 61, 64, 65

An RNA duplex as claimed in the claims mentioned above.  
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7. claims: 39-46

An RNA duplex as claimed in the claims mentioned above.  
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8. claims: 47-54

An RNA duplex as claimed in the claims mentioned above.  
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