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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: OLIGONUCLEOTIDES COMPRISING A NON-PHOSPHATE BACKBONE LINKAGE

(57) Abstract: One aspect of the present invention relates to a ribonucleoside substituted with a phosphoramidite group at the 3'-position. In certain embodiments, the phosphoramidite is an alkyl phosphoramidite. Another aspect of the present invention relates to a double-stranded oligonucleotide comprising at least one non-phosphate linkage. Representative non-phosphate linkages include phosphonate, hydroxylamine, hydroxylhydrazinyl, amide, and carbamate linkages. In certain embodiments, the non-phosphate linkage is a phosphonate linkage. In certain embodiments, a non-phosphate linkage occurs in only one strand. In certain embodiments, a non-phosphate linkage occurs in both strands. In certain embodiments, a ligand is bound to one of the oligonucleotide strands comprising the double-stranded oligonucleotide. In certain embodiments, a ligand is bound to both of the oligonucleotide strands comprising the double-stranded oligonucleotide. In certain embodiments, the oligonucleotide strands comprise at least one modified sugar moiety. Another aspect of the present invention relates to a single-stranded oligonucleotide comprising at least one non-phosphate linkage. Representative non-phosphate linkages include phosphonate, hydroxylamine, hydroxylhydrazinyl, amide, and carbamate linkages. In certain embodiments, the non-phosphate linkage is a phosphonate linkage. In certain embodiments, a ligand is bound to the oligonucleotide strand. In certain embodiments, the oligonucleotide comprises at least one modified sugar moiety.



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**INTERNATIONAL SEARCH REPORT**

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**A. CLASSIFICATION OF SUBJECT MATTER**  
 INV. C12N15/11 C07H21/02 C07H19/167 C07H19/173

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

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, 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	MANOHORAN M ET AL: "Improving Antisense Oligonucleotide Binding to Human Serum Albumin: Dramatic Effect of Ibuprofen Conjugation" CHEMBIOCHEM - A EUROPEAN JOURNAL OF CHEMICAL BIOLOGY, WILEY VCH, WEINHEIM, DE, no. 12, 2002, pages 1257-1260, XP002977263 ISSN: 1439-4227 cited in the application the whole document	85-91, 99-105, 114-140

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	"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
"E" earlier document but published on or after the international filing date	"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
"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)	"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.
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search <b>15 December 2006</b>	Date of mailing of the international search report <b>27/12/2006</b>
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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  <b>Nikolai, Joachim</b>
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## INTERNATIONAL SEARCH REPORT

International application No

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>MANOHARAN M: "Oligonucleotide conjugates as potential antisense drugs with improved uptake, biodistribution, targeted delivery, and mechanism of action"            ANTISENSE &amp; NUCLEIC ACID DRUG DEVELOPMENT, MARY ANN LIEBERT, INC., NEW YORK, US, vol. 12, 2002, pages 103-128, XP002294027            ISSN: 1087-2906            the whole document</p>	1-141
Y	<p>GOODCHILD J: "CONJUGATES OF OLIGONUCLEOTIDES AND MODIFIED OLIGONUCLEOTIDES: A REVIEW OF THEIR SYNTHESIS AND PROPERTIES"            BIOCONJUGATE CHEMISTRY, ACS, WASHINGTON, DC, US, vol. 1, no. 3, May 1990 (1990-05), pages 165-187, XP000174627            ISSN: 1043-1802            pages 167,175,176</p>	1-141
Y	<p>UHLMANN E ET AL: "ANTISENSE OLIGONUCLEOTIDES: A NEW THERAPEUTIC PRINCIPLE"            CHEMICAL REVIEWS, ACS, WASHINGTON, DC, US, vol. 90, no. 4, June 1990 (1990-06), pages 543-544,546, XP002924842            ISSN: 0009-2665            page 565 - page 569</p>	1-141
X	<p>QUARTIN R S ET AL: "NUMBER AND DISTRIBUTION OF METHYLPHOSPHONATE LINKAGES IN OLIGODEOXYNUCLEOTIDES AFFECT EXO- AND ENDONUCLEASE SENSITIVITY AND ABILITY TO FORM RNASE H SUBSTRATES"            NUCLEIC ACIDS RESEARCH, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 17, no. 18, 25 September 1989 (1989-09-25), pages 7253-7262, XP000574936            ISSN: 0305-1048            the whole document</p>	85-95, 99-105, 114-140
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## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2005/023261

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 2004/024919 A (REPLICOR INC [CA]; VAILLANT ANDREW [CA]; JUTEAU JEAN-MARC [CA]) 25 March 2004 (2004-03-25)  paragraphs [0066], [0175], [0179], [0180], [0187]; claims 1,70,75,76; table 1	27-33, 41-46, 50, 54-83, 85-91, 99-105, 114-141
X	paragraphs [0082], [0187], [0188]; claims 11-49; table 1	142,146, 147, 156-161
P,X	US 2005/119214 A1 (MANOHARAN MUTHIAH [US] ET AL) 2 June 2005 (2005-06-02)  paragraphs [0612] - [0618]; claim 32; table 1; compounds AL-DUP-1329	27-34, 38-47, 50,54-83
X	DE 102 00 410 A1 (ROLLER MARC [DE]) 24 July 2003 (2003-07-24)  paragraph [0006]	85-91, 99-105, 114-140
X	paragraphs [0001], [0002]	142-144, 156,158
X	WO 02/098443 A2 (VON DER MUELBE FLORIAN [DE]; HOERR INGMAR [DE]; PASCOLO STEVE [DE] CUR) 12 December 2002 (2002-12-12) claims 1,8; figures 1c-2d; examples 1-4 page 14, line 28 - line 30 page 15, line 15 - line 16	1-161
X	WO 00/28019 A2 (UNIV BEN GURION [IL]; MOR RESEARCH APPLIC LTD [IL]; DOUVDEVANI AMOS [I]) 18 May 2000 (2000-05-18) example examples	85-91, 99-105, 114-140
X	page 5, line 5 - line 10	142,145, 150,151, 156,158
X	WO 01/05963 A2 (UNIV MCGILL [CA]; FUNDYTUS MARIAN E [CA]; CODERRE TERENCE J [CA]; COHE) 25 January 2001 (2001-01-25) examples 1-5	85-91, 99-102, 114-140
X	page 2	142,143, 151-154, 156,158

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## 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 142 - 161 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:

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.:
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.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2005/023261
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