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**WO 01/02423 A3**

(54) Title: 2'-GUANIDINYL-SUBSTITUTED OLIGONUCLEOTIDES AND GENE EXPRESSION MODULATION THERE-  
WITH

(57) Abstract: The present invention provides oligomers which are specifically hybridizable with a selected sequence of RNA or DNA wherein at least one of the nucleoside moieties of the oligomer is modified to include a guanidinium group. These oligomers are useful for diagnostic, therapeutic and investigative purposes.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/18609

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) :Please See Extra Sheet.

US CL :Please See Extra Sheet.

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)

U.S. : 435/6; 514/44; 536/23.1, 24.3, 24.5, 26.7, 26.8, 27.6, 27.8, 27.81, 28.5, 28.53

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
NONE

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

File CAPLUS structure search.

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2,933,502 A (KLOPPING) 19 April 1960, see column 3, line 25.	45-48
X	JP 10081686 A2 (TAKEDA CHEMICAL CO.) 31 March 1998, see English language abstract, structure III.	49-54
X	US 4,977,189 A (TOMCUFCIK et al.) 11 December 1990, see entire document.	45-54
X	DE 33 28 502 A1 (BAYER AG) 14 February 1985, see entire document.	45-54
X	CH 615 157 A5 (BAYER AG) 15 January 1980, see entire document.	49-54
X	CH 612 925 (BAYER AG) 31 August 1979, see entire document.	45-54

 Further documents are listed in the continuation of Box C.
  See patent family annex.

* Special categories of cited documents:	"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
"A" document defining the general state of the art which is not considered to be of particular relevance	"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
"E" earlier document published on or after the international filing date	"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
"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)	"&" document member of the same patent family
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## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/18609

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

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3,993,682 A (KOLLING et al.) 23 November, 1976, see entire document.	45-54
X	JP 48 080560 A2 (SANKYO CO.) 29 October 1973, see English Abstract.	45-54
Y	US 4,794,174 A (SECRIST, III) 27 December 1988, see entire document.	45-54
X	EP 0 850 950 A1 (DAIICHI PHARMACEUTICAL CO) 01 July 1998, see entire document.	49-54
X	FR 2.086.795 (SOCIETE DES USINES CHIMIQUES RHONE-POULENC) 31 December 1971, see entire document.	45-54
X	DE 2 117 293 (RHONE-POULENC S.A.) 21 October 1971, see entire document.	45-54
X	US 3,896,160 A (GAETZI) 22 July 1975, see entire document.	45-54
X	US 2 109 454 (FARBENFABRIKEN BAYER AG) 14 September 1972, see entire document.	45-54
X	DE 2 147 103 (RHONE-POULENC S.A.) 23 March 1972, see entire document.	45-48
X	US 3,929,823 A (BEARD et al.) 30 December 1975, see entire document.	45-48
X	US 3,929,821 A (BEARD et al.) 30 December 1975, see entire document.	45-48
X	US 3,950,395 A (KOLLING et al.) 13 April 1976, see entire document.	45-54
X	US 3,965,113 A (BEARD et al.) 22 June 1976), see column 10.	45-48
X	US 3,812,173 A (GIRAUDON) 21 May 1974, see entire document.	45-54
X	DE 2 250 911 (BAYER AG) 25 April 1974, see entire document.	45-54
X	US 3,929,824 A (BEARD et al.) 30 December 1975, see entire document.	45-48
X	US 3,993,682 A (KOLLING et al.) 23 November 1976, see entire document.	45-54

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/18609

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4,024,176 A (KOLLING et al.) 17 May 1977, see entire document.	45-54
X	US 4,032,655 A (KOLLING et al.) 28 June 1977, see entire document.	45-54

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/18609**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international 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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra 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.:
  
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

International application No.

PCT/US00/18609

A. CLASSIFICATION OF SUBJECT MATTER:

IPC (7):

C12Q 1/68; A61K 31/70; C07H 19/067, 19/073, 19/10, 19/167, 19/173, 19/20, 21/00, 21/02, 21/04

A. CLASSIFICATION OF SUBJECT MATTER:

US CL :

435/6; 514/44; 536/23.1, 24.3, 24.5, 26.7, 26.8, 27.6, 27.8, 27.81, 28.5, 28.53

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claims 1-18, drawn to nucleosides and associated oligonucleotide synthesis precursors wherein the 2'-hydroxyl is replaced by a side chain which has an N-triaminomethyl (N-guanidiny) terminal substituent.

Group II, claims 19-44, drawn to oligonucleotides including 2'-modified nucleotide units.

Group III, claims 45-48, drawn to N, N'-diacyl-S-methylthioureas.

Group IV, claims 49-54, drawn to N-(dihydroxyalkyl)-triaminomethanes.

Group V, claim 55, drawn to solid-support attached N, N'-diacylguanidines.

Group VI, claim 56, drawn to N, N'-diacylguanidiny phosphoramidites.

Group VII, claims 57-58, drawn to methods of modulating gene expression by contacting said gene with a 2'-modified oligonucleotide.

The inventions listed as Groups I, II, III, IV, V, VI and VII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the first six inventions are drawn to chemically distinct species and the seventh invention is directed to a method of nucleic acid hybridization which can be practiced with materially different compounds.