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— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(U))

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Previous Correction:
see Notice of 24 July 2008

(54) Title: POLYMERIC SHORT INTERFERING RNA CONJUGATES

(57) Abstract: The present invention provides polymeric siRNA conjugates. Methods for down-regulation of gene expression in vivo and in vitro and for inhibition of the growth of cancer cells using the conjugates are also disclosed.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US07/85616

A. CLASSIFICATION OF SUBJECT MATTER
 IPC: **C07H 21/04 (2006.01);A61K 31/70 (2006.01)**

 USPC: 536/24.5;5 14/44
 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. : 536/24.5; 514/44

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)
 EAST: siRNA, prodrug, BCL-2, inventor search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category ♦	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
Y	US 2005/0176025 A1 (MCSWIGGEN et al.) 11 August 2005 (11.08.2005), see entire document.	1-33
Y	US 2004/0235773 A1 (ZHAO et al.) 25 November 2004 (25.11.2004), see entire document.	1-33

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 application or patent 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		
"P" document published prior to the international filing date but later than the priority date claimed	"&"	document member of the same patent family

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Name and mailing address of the ISA/US: Mail Stop PCT, Ann ISA/US, Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450, Facsimile No. (571) 273-3201
 Authorized officer: Tracy Vivlemore, Telephone No. 571-272-1600

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:
Please See Continuation Sheet

1. I I As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. XJ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. I I 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 and, where applicable, the payment of a protest fee.
- I I 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.
- I I No protest accompanied the payment of additional search fees.

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows: the structures of releasable or permanent linkers designated as R2 shown in claims 6-9, 22 and 23.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: each of the specific R2 structures shown has distinct chemical structural components.