



(51) International Patent Classification:

C07K 19/00 (2006.01) A61P 35/00 (2006.01)

(21) International Application Number:

PCT/US2009/030164

(22) International Filing Date:

5 January 2009 (05.01.2009)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/019,244	5 January 2008 (05.01.2008)	US
61/027,100	8 February 2008 (08.02.2008)	US

(71) Applicant (for all designated States except US):
SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH [US/US]; Office of Industrial Affairs 1275 York Avenue, New York, New York 10065 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BENEZRA, Robert** [US/US]; 402 E. 64th Street, Apt. 7C, New York, New York 10065 (US). **HENKE, Erik** [DE/US]; 475 Main Street, Apt 9B, New York, New York 10044 (US).

(74) Agent: **LARSON, Marina, T., Ph.D.**; Larson & Anderson, LLC, P.O. Box 4928, Dillon, Colorado 80435 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,

CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))

(88) Date of publication of the international search report:

24 September 2009

(54) Title: PEPTIDE-CONJUGATED OLIGONUCLEOTIDE THERAPEUTIC AND METHOD OF MAKING AND USING SAME

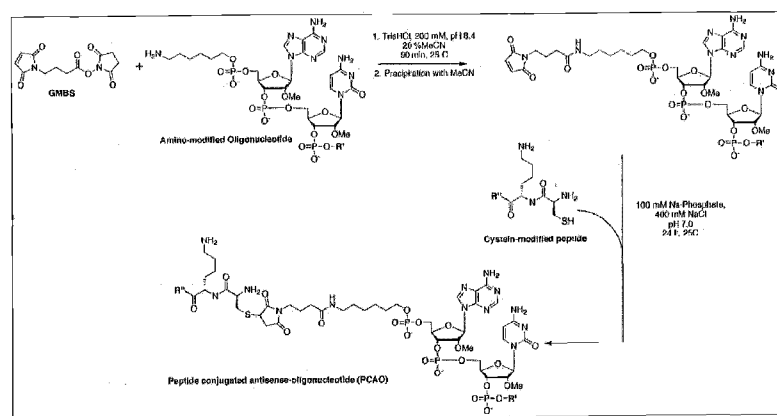


Fig. 1

(57) Abstract: Conjugates for the efficient delivery of sequence-specific antisense to cells of a selected type for the inhibition of a target protein have the general formula: peptide-HBL-antisense in which the peptide is a homing peptide which directs the conjugate to cells of a particular type, antisense is an antisense oligonucleotide having a sequence selected to provide sequence-specific inhibition of the target protein, and HBL is a heterobifunctional linker having reactivity towards amino and sulfhydryl groups.

A. CLASSIFICATION OF SUBJECT MATTER***C07K 19/00(2006.01)i, A61P 35/00(2006.01)i***

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)

IPC A61K 47/48, C07K 19/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Korean Utility Models and applications for Utility Models since 1975

Japanese Utility Models and applications for Utility Models since 1975

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

eKOMPASS(KIPO internal) & keyword: peptide, HBL, antisense, oligonucleotide, conjugate, linker, cancer, tumor, sulfhydryl, and heterobifunctional

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96-06641 A1 (PRIZM PHARMACEUTICALS, INC.) 07 Mar 1996 See the whole document, especially, abstract, claims 1, 2, 13	1-25
A	TONG- YOUNG LEE et al. Peptide-mediated targeting to tumor blood vessels of lung cancer for drug delivery. Cancer Res. 15 Nov 2007, Vol. 67, No. 22, pages 10958-10965 See the whole document, especially, abstract, pages 10960-10962	1-25
A	MARVIN RUBENSTEIN et al. Construction of a bispecific antisense oligonucleotide containing multiple binding sites for the treatment of hormone insensitive prostate tumors. Medical Hypotheses. 2005, Vol. 65, pages 905-907 See the whole document	1-25
A	DMITRI A.A. VANDEPUTTE et al. Expression and distribution of Id helix-loop-helix proteins in human astrocytic tumors. GLIA. 2002, Vol. 38, pages 329-338 See the whole document	1-25



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 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

27 JULY 2009 (27.07.2009)

Date of mailing of the international search report

28 JULY 2009 (28.07.2009)

Name and mailing address of the ISA/KR

Korean Intellectual Property Office
Government Complex-Daejeon, 139 Seonsa-ro, Seo-
gu, Daejeon 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

Chio Jun Ho

Telephone No. 82-42-481-5569



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2009/030164

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	ERIK HENKE et al. Peptide-conjugated antisense oligonucleotides for targeted inhibition of a transcriptional regulator in vivo. Nature Biotechnology. 06 Jan 2008, Vol. 26, No. 1, pages 91-100 See the whole document, especially, abstract, figure 1, pages 92, 94, 95	1, 2, 4, 6, 9, 11, 14, 16, 19, 21

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2009/030164**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.: 26-37
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 26-37 pertain to method for treatment of the human or animal body by therapy, as well as diagnostic methods, and thus relate to a subject matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.
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:

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 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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2009/030164

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 96-06641 A1	07.03.1996	AU 710309 B2	16.09.1999
		AU 1999-62380 B2	01.06.1999
		AU 1999-62380 A1	01.06.1999
		AU 702323 B2	18.02.1999
		AU 765436 B2	18.09.2003
		AU 1996-58628 B2	16.05.1996
		AU 1995-22724 B2	15.03.1995
		CA 2330026 A1	29.12.1999
		EP 1188448 A3	17.04.2002
		EP 1082142 A2	14.03.2001
		EP 1188448 A2	20.03.2002
		JP 2002-518464 A	25.06.2002
		JP 11-505805 A	25.05.1999
		JP 09-510352 A	21.10.1997
		US 2003-0040496 A1	27.02.2003
		US 06037329 A	14.03.2000
		US 06551618 B2	22.04.2003
		US 2002-0168338 A1	14.11.2002
		US 2004-0138155 A1	15.07.2004
		US 2008-0152689 A1	26.06.2008
		US 07138381 B2	21.11.2006
		US 06503886 B1	07.01.2003
		US 2003-0143217 A1	31.07.2003
		WO 1996-008274 A3	21.03.1996
		WO 1995-024928 A3	21.09.1995
		WO 1996-036362 A1	21.11.1996
		WO 1999-066959 A2	29.12.1999
		WO 1999-066959 A3	29.12.1999