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(54) Title: CHIMERIC snRNA MOLECULES CARRYING ANTISENSE SEQUENCES AGAINST THE SPLICE JUNCTIONS OF THE DYSTROPHIN GENE AND THEIR THERAPEUTIC APPLICATIONS

(57) Abstract: A gene is described that encodes for a snRNA modified such that it contains an antisense sequence complementary to at least one of the two splice junctions at 5' and/or 3' of one of the exons encoding for a protein of therapeutic interest, whose sequence should be skipped during the splicing process that converts the pre-mRNA to the mature mRNA. The gene is particularly advantageous which it contain segments complementary to both splice junctions. If introduced into appropriate vectors, the gene is useful in gene therapy, particularly in the treatment of Duchenne Muscular Dystrophies, dystrophic diseases.



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INTERNATIONAL SEARCH REPORT

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PCT/IT 03/00273

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C12N15/11 A61K48/00

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 7 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)

WPI Data, EPO-Internal, BIOSIS, MEDLINE, SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>GORMAN ET AL.: "Restoration of Correct Splicing of Thalassemic β-Globin Pre-mRNA by modified U1 snRNAs"</p> <p>J BIOL CHEM, vol. 275, no. 46, 17 November 2000 (2000-11-17), pages 35914-35919, XP002261981 cited in the application abstract; figure 1</p>	1-6, 13, 14
Y	<p>the whole document</p> <p>---</p> <p>-/--</p>	7-12, 15, 16

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/IT 03/00273

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	M. MATSUO: "Duchenne and Becker Muscular Dystrophy: From Gene Diagnosis to Molecular Therapy" IUBMB LIFE, vol. 53, no. 3, March 2002 (2002-03), pages 147-152, XP009021242 Summary; Figure 1; Table 1 ---	7-12,15, 16
Y	EP 1 191 097 A (LEIDS UNI MEDISCH CT) 27 March 2002 (2002-03-27) claims 1-6 ---	7-12,15, 16
Y	DEUTEKOM VAN J C T ET AL: "Antisense-induced exon skipping restores dystrophin expression in DMD patient derived muscle cells" HUMAN MOLECULAR GENETICS, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 10, no. 15, 2001, pages 1547-1554, XP002250908 ISSN: 0964-6906 the whole document ---	7-12,15, 16
Y	MANN C J ET AL: "ANTISENSE-INDUCED EXON SKIPPING AND SYNTHESIS OF DYSTROPHIN IN THE MDX MOUSE" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 98, no. 1, 2 January 2001 (2001-01-02), pages 42-47, XP001160821 ISSN: 0027-8424 cited in the application abstract page 46-47 ---	7-12,15, 16
A	SUTER D ET AL: "DOUBLE-TARGET ANTISENSE U7 SNRNAS PROMOTE EFFICIENT SKIPPING OF AN ABERRANT EXON IN THREE HUMAN BETA-THALASSEMIC MUTATIONS" HUMAN MOLECULAR GENETICS, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 8, December 1999 (1999-12), pages 2415-2423, XP000973208 ISSN: 0964-6906 cited in the application the whole document --- -/--	1-16

INTERNATIONAL SEARCH REPORT

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PCT/IT 03/00273

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	<p>DE ANGELIS FERNANDA GABRIELLA ET AL: "Chimeric snRNA molecules carrying antisense sequences against the splice junctions of exon 51 of the dystrophin pre-mRNA induce exon skipping and restoration of a dystrophin synthesis in Delta 48-50 DMD cells." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA. UNITED STATES 9 JUL 2002, vol. 99, no. 14, 9 July 2002 (2002-07-09), pages 9456-9461, XP002261982 ISSN: 0027-8424 the whole document</p> <p>----</p>	1-16
P,X	<p>BRUN C ET AL: "U7 snRNAs induce correction of mutated dystrophin pre-mRNA by exon skipping." CMLS CELLULAR AND MOLECULAR LIFE SCIENCES, vol. 60, no. 3, March 2003 (2003-03), pages 557-566, XP009021235 ISSN: 1420-682X the whole document</p> <p>-----</p>	1-4

INTERNATIONAL SEARCH REPORT
Information on patent family members

International Application No
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			EP 1320597 A2	25-06-2003
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