

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
26 October 2000 (26.10.2000)

PCT

(10) International Publication Number
WO 00/62736 A3

(51) International Patent Classification⁷: A01N 43/04,
A61K 31/70, C12Q 1/68, C07H 21/02, 21/04, 19/20

(21) International Application Number: PCT/US00/08020

(22) International Filing Date: 24 March 2000 (24.03.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/127,958 6 April 1999 (06.04.1999) US

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(81) Designated States (national): AL, AM, AT, AU, AZ, BA,
BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES,
FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG,
MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN,
YU, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,
KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent
(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent
(AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,
MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

(88) Date of publication of the international search report:
11 October 2001

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: LOW ADENOSINE ANTI-SENSE OLIGONUCLEOTIDE, COMPOSITIONS, KIT AND METHOD FOR TREATMENT OF AIRWAY DISORDERS ASSOCIATED WITH BRONCHOCONSTRICTION, LUNG INFLAMMATION, ALLERGY(IES) AND SURFACTANT DEPLETION

(57) Abstract: An in vivo method of selectively delivering a nucleic acid to a target gene or mRNA comprises the topical administration, e.g. to the respiratory system, of a subject of a therapeutic amount of an oligonucleotide that is antisense to the initiation codon region, coding region, 5' or 3' in-ton-exon junctions or regions within 2 to 10 nucleotides of the junctions of the target gene, or antisense to a mRNA complementary to the target gene in an amount effective to reach the target polynucleotide and reducing or inhibiting expression. Additionally, a method of treating and adenosine mediated effect is described also utilizing the delivery of antisense and in order to minimize triggering adenosine receptors by their metabolism, the administered oligos have a low content of or are essentially free of adenosine. The agent, composition and formulations are used for prophylactic, preventive and therapeutic treatment of ailments associated with impaired respiration, lung allergies and/or vasoconstriction, inflammation, allergies, allergic rhinitis, asthma, impeded respiration, lung pain, cystic fibrosis and bronchoconstriction.



WO 00/62736 A3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/08020

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A01N 43/04; A61K 31/70; C12Q 1/68; C07H 21/02, 21/04, 19/20

US CL : 514/44, 46; 435/6, 455, 468, 366, 375; 536/23.1, 24.5, 26.71

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. : 514/44, 46; 435/6, 455, 468, 366, 375; 536/23.1, 24.5, 26.71

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

Parent Case: 60/127,958

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

Dialog, West

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X, P	US 6,017,898 A (PIETRZKOWSKI et al.) 25 January 2000, entire text, especially col. 3, line 51-col. 4, line 35.	1, 3, 4, 5, 17, 19, 20, 25, 26, 50-52
A, P	US 5,994,315 A (NYCE et al.) 30 November 1999, entire text.	1-83, 85-91
A, P	US 6,025,339 A (NYCE) 15 February 2000, entire text.	1-83, 85-91
Y	WO 99/11275 A2 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) 11 March 1999, page 15, lines 1-page 17, line 9.	10, 65, 71
A	NYCE, J. W. Insight into adenosine receptor function using antisense and gene-knockout approaches. Trends in Pharmacological Sciences. February 1999, Vol. 20, No. 2, pages 79-83.	1-83, 85-91

 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
I 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)	*Z* document member of the same patent family
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	

Date of the actual completion of the international search

29 JUNE 2000

Date of mailing of the international search report

09 AUG 2000

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/08020

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	RICHARDSON, P. J. Blocking adenosine with antisense. Nature. February 1997, Vol. 385, pages 684-685.	1-5, 50-53
X --- Y	NYCE et al. DNA antisense therapy for asthma in an animal model. Nature. February 1997, Vol. 385, pages 721-724.	1-5, 10, 12, 13, 17-20, 22, 24, 26- 30, 39, 43, 50-53, 55-57, 61, 62, 64- 66, 72, 76-79, 83, 86 ----- 16, 23, 30-38, 40- 49, 54, 59, 60, 73-75, 80-82, 85, 87, 89, 91
A	CROOKE, S. T. Antisense Research and Application. Germany: Springer-Verlag. 1997, Chapter 1, 'Basic Principles of Antisense Therapeutics', pages 1-50.	1-83, 85-91
Y	SANGHVI, Y. S. Antisense Research and Applications. CRC Press, Inc. 1993, Chapter 15, 'Heterocyclic Base Modifications in Nucleic Acids and Their Applications in Antisense Oligonucleotides', pages 273-288, see entire document.	7-9, 11, 67-70
Y	US 5,801,154 A (BARACCHINI et al.) 01 September 1998, col. 6, line 18-col. 8, line 56.	7-9, 11, 12, 15, 16, 67-70, 72-74

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/08020**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.: 84
because they relate to subject matter not required to be searched by this Authority, namely:

No computer readable form of the sequences cited in this claim was available to be searched.
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:

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.