

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
6 March 2003 (06.03.2003)

PCT

(10) International Publication Number
WO 03/018600 A3

(51) International Patent Classification⁷: **C07H 21/04**,
A61K 48/00, C12N 15/00

(21) International Application Number: PCT/US02/22799

(22) International Filing Date: 17 July 2002 (17.07.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/917,963 30 July 2001 (30.07.2001) US

(71) Applicant (*for all designated States except US*): **ISIS PHARMACEUTICALS, INC.** [US/US]; 2292 Faraday Avenue, Carlsbas, CA 92008 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **CROOKE, Rosanne, M.** [US/US]; 3211 Piraqua Street, Carlsbad, CA 92009 (US). **GRAHAM, Mark, J.** [US/US]; 2305 S. Ola Vista, San Clemente, CA 92672 (US).

(74) Agents: **LICATA, Jane, Massey** et al.; Licata & Tyrrel P.C., 66 E. Main Street, Marlton, NJ 08053 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, 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, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

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

Published:

— with international search report

(88) Date of publication of the international search report:
30 October 2003

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: ANTISENSE MODULATION OF MICROSOMAL TRIGLYCERIDE TRANSFER PROTEIN EXPRESSION

(57) Abstract: Antisense compounds, compositions and methods are provided for modulating the expression of microsomal triglyceride transfer protein. The compositions comprise antisense compounds, particularly antisense oligonucleotides, targeted to nucleic acids encoding microsomal triglyceride transfer protein. Methods of using these compounds for modulation of microsomal triglyceride transfer protein expression and for treatment of diseases associated with expression of microsomal triglyceride transfer protein are provided.



WO 03/018600 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/22799

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07H 21/04; A61K 48/00; C12N 15/00

US CL : 435/375, 377; 536/24.5; 514/44

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. : 435/375, 377; 536/24.5; 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONEElectronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WEST, MEDLINE, BIOSIS, SCISEARCH, CAPLUS, BIOTECHNO, EMBASE**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BIESSEN et al. Novel Potent Antisense Drugs for Down-Regulating Murine MTP Expression: Potential in Hypocholesterolemic Therapy. Circulation. 31 October 2000, Vol. 102, No. 18, Suppl. II, page 148, see entire abstract No. 721.	1-20
Y	US 5,595,872 A (WETTERAU, II et al) 21 January 1997, see especially columns 52-53.	1-20



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	"&" document member of the same patent family
"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

18 September 2002 (18.09.2002)

Date of mailing of the international search report

29 NOV 2002

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703)305-3230

Authorized officer

Seth R. McGarry

Telephone No. (703) 308-0196