(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
5 August 2004 (05.08.2004)

PCT

(10) International Publication Number
WO 2004/065620 A3

(51) International Patent Classification[7]: A61K 31/70, C07H 21/04, C12Q 1/68

(21) International Application Number: PCT/US2004/000801

(22) International Filing Date: 13 January 2004 (13.01.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10/346,268 15 January 2003 (15.01.2003) US

(71) Applicant *(for all designated States except US)*: **ISIS PHARMACEUTICALS, INC.** [US/US]; 1896 Rutherford Road, Carlsbad, CA 92008 (US).

(72) Inventors: **BENNETT, C., Frank**; 1347 Cassins Street, Carlsbad, CA 92009 (US). **DEAN, Nicholas, M.**; 2110 Whisperwind Lane, Olivenhain, CA 92024 (US). **DOBIE, Kenneth, W.**; 703 Stratford Ct. #4, Del Mark, CA 92014 (US). **JAIN, Ravi**; 6520 Ambrosia Lane, #1227, Carlsbad, CA 92009 (US).

(74) Agents: **SHUSTER, Michael, J.** et al.; Fenwick & West LLP, 801 California Street, Mountain View, CA 94041 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, 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, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, 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, HU, IE, IT, LU, MC, NL, 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*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report: 22 September 2005

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: MODULATION OF THYROID HORMONE RECEPTOR INTERACTOR 3 EXPRESSION

(57) Abstract: Compounds, compositions and methods are provided for modulating the expression of thyroid hormone receptor interactor 3. The compositions comprise oligonucleotides, targeted to nucleic acid encoding thyroid hormone receptor interactor 3. Methods of using these compounds for modulation of thyroid hormone receptor interactor 3 expression and for diagnosis and treatment of disease associated with expression of thyroid hormone receptor interactor 3 are provided.

WO 2004/065620 A3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/00801

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : A61K 31/70; C07H 21/04; C12Q 1/68
US CL : 536/24.5; 514/44; 435/6, 325, 375
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; 435/6, 325, 375

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)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2000/29623 A2 (CURAGEN CORP.) 25 May 2000 (25.05.2000), see page 498.	1-6, 9-13
Y	US 5,998,148 A (BENNETT et al.) 07 December 1999 (07.12.1999), col. 5-7.	1-20, 22
Y	TAYLOR et al. Antisense oligionucleotides: a systematic high-throughput approach to target validation and gene function determination. Drug Design Today. December 1999, Vol. 4, No. 12, pages 562-567, especially pages 562, and 565.	1-20, 22
Y	WO 98-49561 A1 (IMPERIAL CANCER RESEARCH TECHNOLOGY LIMITED) 05 November 1998 (05.11.1998), see page 2.	1-20, 22
Y	GenBank Accession No. L40410.1 15 March 1995 (15.03.1995).	1-20, 22
Y	IWAHASHI et al. Thyroid Hormone Receptor Interacting Protein 3 (TRIP3) Is a Novel Coactivator of Hepatocyte Nuclear Factor-4-alpha. Diabetes, April 2002, Vol. 51, pages 910-914, especially page 911.	1-20, 22

☒ 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 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 another 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	Date of mailing of the international search report
26 June 2005 (26.06.2005)	15 JUL 2005
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Janet L. ~~Epps-Ford, Ph.D.~~ Telephone No. 571-272-0547

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/00801

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BRAASCH et al. Novel Antisense and Peptide Nucleic Acid Strategies for Controlling Gene Expression. Biochemistry. March 2002, Vol. 41, No. 14. pages 4503-4510, see page 4506.	18 and 23-27

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/00801

Continuation of B. FIELDS SEARCHED Item 3:
CAplus, Registry, USpatfull, US-PG-pub, USPAT, EPO, JPO, Derwent
search terms: TRIP3, thyroid hormone receptor interactor 3, antisense, siRNA, dsRNA, ribozyme,inhibitor.