

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

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
3 January 2002 (03.01.2002)

PCT

(10) International Publication Number
WO 02/00716 A3

- (51) International Patent Classification⁷: C12N 5/10, C12Q 1/66, G01N 33/50, C07K 14/72
- (21) International Application Number: PCT/US01/19609
- (22) International Filing Date: 20 June 2001 (20.06.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/214,392 28 June 2000 (28.06.2000) US
- (71) Applicant (for all designated States except US): BRISTOL-MYERS SQUIBB COMPANY [US/US]; P.O. Box 4000, Lawrenceville-Princeton Road, Princeton, NJ 08543 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): OSTROWSKI, Jacek [US/US]; 2445 Primrose Court, Jamison, PA 18929 (US). DRISCOLL, Joyce [US/US]; 133 Riverwoods Drive, New Hope, PA 18938 (US). LUPISELLA, John [US/US]; 230 Riverwoods Drive, New Hope, PA 18938 (US). SALVATI, Mark [US/US]; 9 Tracey Drive, Lawrenceville, NJ 08648 (US).
- (74) Agents: SWITZER, Joan, E. et al.; Bristol-Myers Squibb Company, P.O. Box 4000, Lawrenceville-Princeton Road, Princeton, NJ 08543 (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, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, 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, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, 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:
13 June 2002

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: CELL LINES AND CELL-BASED ASSAYS FOR IDENTIFICATION OF ANDROGEN RECEPTOR MODULATORS

(57) Abstract: Stable muscle cell lines comprising an androgen receptor and methods of using these cells in functional transactivation assays to assess the efficacy of compounds as androgen receptor modulators in a muscle cell background are provided.



WO 02/00716 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/19609

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N5/10 C12Q1/66 G01N33/50 C07K14/72

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 C12Q C07K

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)

EPO-Internal, INSPEC, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TABB JOEL S ET AL: "Suppression of sodium channel function in differentiating C2 muscle cells stably overexpressing rat androgen receptors." JOURNAL OF NEUROSCIENCE, vol. 14, no. 2, 1994, pages 763-773, XP001056898 ISSN: 0270-6474	1-3
Y	the whole document ----- -/--	4-10,13, 15,17,19

Further documents are listed in the continuation of box C.

Patent family members are listed in 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 document 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 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

15 March 2002

Date of mailing of the international search report

08/04/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Marinoni, J-C

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/19609

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>GERDES MICHAEL J ET AL: "Transforming growth factor-beta1 induces nuclear to cytoplasmic distribution of androgen receptor and inhibits androgen response in prostate smooth muscle cells." ENDOCRINOLOGY, vol. 139, no. 8, August 1998 (1998-08), pages 3569-3577, XP002193244 ISSN: 0013-7227 the whole document</p> <p>---</p>	1,3
X	<p>SYMS A J ET AL: "MECHANISM OF ANDROGEN-RECEPTOR AUGMENTATION ANALYSIS OF RECEPTOR SYNTHESIS AND DEGRADATION BY THE DENSITY-SHIFT TECHNIQUE" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 260, no. 1, 1985, pages 455-461, XP001057030 ISSN: 0021-9258 the whole document</p> <p>---</p>	1,3
Y	<p>WO 96 40958 A (BAYLOR COLLEGE MEDICINE) 19 December 1996 (1996-12-19) the whole document</p> <p>---</p>	1-10,13, 15,17,19
Y	<p>WO 92 16546 A (SALK INST FOR BIOLOGICAL STUDI) 1 October 1992 (1992-10-01) the whole document</p> <p>---</p>	1-10,13, 15,17,19
Y	<p>WO 88 03168 A (SALK INST FOR BIOLOGICAL STUDIES) 5 May 1988 (1988-05-05) the whole document</p> <p>---</p>	1-10,13, 15,17,19
Y	<p>YARBROUGH W G ET AL: "A SINGLE BASE MUTATION IN THE ANDROGEN RECEPTOR GENE CAUSES ANDROGEN INSENSITIVITY IN THE TESTICULAR FEMINIZED RAT" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 265, no. 15, 1990, pages 8893-8900, XP001062675 ISSN: 0021-9258 the whole document</p> <p>---</p>	1-10,13, 15,17,19
Y	<p>TEROUANNE BEATRICE ET AL: "A stable prostatic bioluminescent cell line to investigate androgen and antiandrogen effects." MOLECULAR AND CELLULAR ENDOCRINOLOGY, vol. 160, no. 1-2, 25 February 2000 (2000-02-25), pages 39-49, XP002193245 ISSN: 0303-7207 the whole document</p> <p>---</p>	1-10,13, 15,17,19
	-/--	

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/19609

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>HOFBAUER LORENZ C ET AL: "Development and characterization of a conditionally immortalized human osteoblastic cell line stably transfected with the human androgen receptor gene." JOURNAL OF CELLULAR BIOCHEMISTRY, vol. 66, no. 4, 1997, pages 542-551, XP002193246 ISSN: 0730-2312 the whole document</p>	1-10,13, 15,17,19
Y	<p>FUHRMANN U ET AL: "STABLE TRANSFECTION OF ANDROGEN RECEPTOR AND MMTV-CAT INTO MAMMALIAN CELLS: INHIBITION OF CAT EXPRESSION BY ANTI-ANDROGENS" JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, ELSEVIER SCIENCE LTD., OXFORD, GB, vol. 42, no. 8, September 1992 (1992-09), pages 787-793, XP000884986 ISSN: 0960-0760 the whole document</p>	1-10,13, 15,17,19
Y	<p>EVANS R M: "THE STERIOD AND THYROID HORMONE RECEPTOR SUPERFAMILY" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE, US, vol. 240, no. 4854, 13 May 1988 (1988-05-13), pages 889-895, XP000574469 ISSN: 0036-8075 cited in the application the whole document</p>	1-10,13, 15,17,19
Y	<p>ZHOU ZHIFENG ET AL: "Identification and characterization of a novel androgen response element composed of a direct repeat." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 272, no. 13, 1997, pages 8227-8235, XP002193247 ISSN: 0021-9258 the whole document</p>	1-10,13, 15,17,19
P,X	<p>SALM SARAH N ET AL: "Transforming growth factor-beta is an autocrine mitogen for a novel androgen-responsive murine prostatic smooth muscle cell line, PSMC1." JOURNAL OF CELLULAR PHYSIOLOGY, vol. 185, no. 3, December 2000 (2000-12), pages 416-424, XP001056974 ISSN: 0021-9541 the whole document</p>	1

-/--

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/19609

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 54728 A (NOVALON PHARMACEUTICAL CORP ;BARNETT TOM (US); FOWLKES DANA M (US)) 28 October 1999 (1999-10-28) the whole document	
A	--- NEGRO-VILAR ANDRES: "Selective androgen receptor modulators (SARMs): A novel approach to androgen therapy for the new millennium." JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM, vol. 84, no. 10, October 1999 (1999-10), pages 3459-3462, XP002193249 ISSN: 0021-972X cited in the application -----	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 11, 12, 14, 16, 18, 20 all completely

Present claims 11 and 12 relate to completely undefined cell lines since the ATCC deposit number is mentioned neither in the description nor in the claims. Consequently, a lack of clarity within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible.

Present claims 14, 16, 18 and 20 relate to an extremely large number of possible compounds. These compounds are defined in the description by the result to be achieved (see page 17, lines 13-19), i.e. their antagonist effect but are not characterized by technical features. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for none of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the claimed scope is impossible.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/19609

Patent document cited in search report	A	Publication date	Patent family member(s)	Publication date			
WO 9640958	A	19-12-1996	AU 705035 B2	13-05-1999			
			AU 5714296 A	30-12-1996			
			CA 2222550 A1	19-12-1996			
			EP 0832269 A1	01-04-1998			
			JP 11506722 T	15-06-1999			
			WO 9640958 A1	19-12-1996			
			<hr style="border-top: 1px dashed black;"/>				
WO 9216546	A	01-10-1992	AT 199169 T	15-02-2001			
			AU 668683 B2	16-05-1996			
			AU 1657892 A	21-10-1992			
			CA 2100584 A1	20-09-1992			
			DE 69231689 D1	22-03-2001			
			DE 69231689 T2	28-06-2001			
			EP 0576590 A1	05-01-1994			
			JP 6508509 T	29-09-1994			
			WO 9216546 A1	01-10-1992			
			<hr style="border-top: 1px dashed black;"/>				
			WO 8803168	A	05-05-1988	US 5071773 A	10-12-1991
AT 182173 T	15-07-1999						
AU 616389 B2	31-10-1991						
AU 8238887 A	25-05-1988						
DE 3752284 D1	19-08-1999						
DE 3752284 T2	25-11-1999						
EP 0287653 A1	26-10-1988						
EP 0733705 A1	25-09-1996						
JP 10004987 A	13-01-1998						
JP 10108684 A	28-04-1998						
JP 11137272 A	25-05-1999						
JP 1500964 T	06-04-1989						
JP 2001069998 A	21-03-2001						
WO 8803168 A1	05-05-1988						
US 5597705 A	28-01-1997						
US 5534418 A	09-07-1996						
US 5606021 A	25-02-1997						
US 5312732 A	17-05-1994						
US 5298429 A	29-03-1994						
<hr style="border-top: 1px dashed black;"/>							
WO 9954728	A	28-10-1999	AU 3209199 A	08-11-1999			
			EP 1073891 A2	07-02-2001			
			WO 9954728 A2	28-10-1999			