(19) World Intellectual Property Organization International Bureau





(43) International Publication Date 18 July 2002 (18.07.2002)

PCT

(10) International Publication Number WO 02/055742 A3

(51) International Patent Classification⁷: G01N 33/50, C12Q 1/68

(21) International Application Number: PCT/EP02/00106

(22) International Filing Date: 8 January 2002 (08.01.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/260,571 9 January 2001 (09.01.2001) US 60/302,614 2 July 2001 (02.07.2001) US

(71) Applicant (for all designated States except AT, US): NO-VARTIS AG [CH/CH]; Lichstrasse 35, CH-4056 Basel (CH).

(71) Applicant (for AT only): NOVARTIS PHARMA GMBH [AT/AT]; Brunner Strasse 59, A-1230 Vienna (AT).

(72) Inventor; and

(75) Inventor/Applicant (for US only): LASSOTA, Piotr [US/US]; 99 South Hillside Avenue, Succasunna, NJ 07876 (US).

(74) Agent: BECKER, Konrad; Novartis AG, Corporate Intellectual Property, Patent & Trademark Department, CH-4002 Basel (CH).

(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, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): 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).

Published:

with international search report

(88) Date of publication of the international search report:
4 September 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: RAPID METHOD FOR SCREENING COMPOUNDS FOR IN VIVO ACTIVITY

(57) Abstract: The present invention provides a rapid method for screening potentially pharmaceutically useful compounds for activity *in vivo*. The method has the steps of growing a target cell into which a reporter gene was introduced in a biocompatible, semipermeable encapsulation device; implanting the semi-permeable encapsulation device into a subject; administering a potentially pharmaceutically active compound to said subject; removing said encapsulation device from said subject after *in vivo* exposure to the potentially pharmaceutically active compound and evaluating said target cell for reaction to said potentially paharmaceutically active compound by measuring the expression of said reporter gene.

INTERNATIONAL SEARCH REPORT

Internal Application No PCT/EP 02/00106

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 G01N33/50 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

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)

BIOSIS, EPO-Internal, WPI Data, EMBASE

C. DOCUME	ENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
Υ	WO 94 25074 A (US HEALTH) 10 November 1994 (1994-11-10) page 6, line 1 -page 11, line 21; claims 1-20	1–17	
Y	WO 94 16080 A (EXEMPLAR CORP) 21 July 1994 (1994-07-21) page 7, paragraph 1 page 8, paragraph 2 -page 10, paragraph 1 page 13, paragraph 4 -page 16, paragraph 2; claims 1-45	1–17	
Y	EP 0 218 400 A (DAMON BIOTECH INC) 15 April 1987 (1987-04-15) page 2, line 41 -page 3, line 8; claims 1-14; examples 1-7	1-17	

Further documents are listed in the continuation of box C.	χ 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	Date of mailing of the international search report
29 April 2003	15/05/2003
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2	Authorized officer
NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Bradbrook, D

INTERNATIONAL SEARCH REPORT

Intermenal Application No
PCT/EP 02/00106

		PCT/EP 02/00106
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Υ	CASCIARI JOSEPH J ET AL: "Growth and chemotherapeutic response of cells in a hollow-fiber in vitro solid tumor model." JOURNAL OF THE NATIONAL CANCER INSTITUTE (BETHESDA), vol. 86, no. 24, 1994, pages 1846-1852, XP009009925 ISSN: 0027-8874 abstract page 1847, column 1, paragraph 2 -column 2, paragraph 2 page 1851, column 3, paragraph 2	1-17
Y	HOLLINGSHEAD MELINDA ET AL: "In vivo drug screening applications of HIV-infected cells cultivated within hollow fibres in two physiologic compartments of mice." ANTIVIRAL RESEARCH, vol. 28, no. 3, 1995, pages 265-279, XP002239733 ISSN: 0166-3542 abstract page 267, paragraphs 1-4 page 275, paragraph 2 -page 277, paragraph 2	1-17
Υ	HOLLINGSHEAD M ET AL: "The hollow fiber assay." 1999 , CONTRIBUTIONS TO ONCOLOGY, VOL. 54, PAGE(S) 109-120 , DRUG DEVELOPMENT. 1999 S. KARGER GMBH POSTFACH, D-79095, FREIBURG, GERMANY XP009009927 ISBN: 3-8055-6786-3 page 109, paragraph 1 -page 113, paragraph 1	1-17

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 1-17 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the method.

Continuation of Box I.1

Claims Nos.: 1-17 (partially)

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery/therapy (claims 1-17)



Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: 1-17 (partially) because they relate to subject matter not required to be searched by this Authority, namely: See FURTHER INFORMATION sheet PCT/ISA/210
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.

INTERNATIONAL SEARCH REPORT

ormation on patent family members

PCT/EP 02/00106

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9425074	A	10-11-1994	US AU AU EP JP WO	5698413 A 697146 B2 6711594 A 0697892 A1 8512292 T 9425074 A1	16-12-1997 01-10-1998 21-11-1994 28-02-1996 24-12-1996 10-11-1994
WO 9416080	Α	21-07-1994	AU WO	5965294 A 9416080 A1	15-08-1994 21-07-1994
EP 0218400	А	15-04-1987	AT AU AU CA DE EP JP NO	58840 T 571144 B2 6279786 A 1265443 A1 3676036 D1 0218400 A1 62122598 A 863719 A	15-12-1990 31-03-1988 19-03-1987 06-02-1990 17-01-1991 15-04-1987 03-06-1987 19-03-1987