(19) World Intellectual Property Organization

International Bureau





(43) International Publication Date 3 May 2001 (03.05.2001)

PCT

(10) International Publication Number WO~01/30802~A3

(51) International Patent Classification⁷: A61K 31/565, 31/566, A61P 7/06

(21) International Application Number: PCT/US00/26771

(22) International Filing Date:

28 September 2000 (28.09.2000)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/161,453

25 October 1999 (25.10.1999) US

(71) Applicant: HOLLIS-EDEN PHARMACEUTICALS, INC. [US/US]; Suite 200, 9333 Genesee Avenue, San Diego, CA 92121 (US).

(72) Inventors: FRINCKE, James, Martin; P.O. Box 927420, San Diego, CA 92192 (US). READING, Christopher, L.; P.O. Box 12511, San Diego, CA 92112-3511 (US). PREN-DERGAST, Patrick, T.; Baybush, Straffan, County Kildare (IE).

(74) Agent: HUNT, Dale, C.; 16th floor, 620 Newport Center Drive, Newport Beach, CA 92660 (US).

- (81) Designated States (national): AE, AG, AL, AM, AT, AT (utility model), AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ (utility model), DE, DE (utility model), DK, DK (utility model), DM, DZ, EE, EE (utility model), ES, FI, Fl (utility model), GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR (utility model), 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, SK (utility model), SL, TJ, TM, TR, TT, TZ, UA, UG, 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), 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: 14 February 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.

(7

802 A

(54) Title: THERAPEUTIC TREATMENTS COMPRISING ADMINISTRATION OF CERTAIN STEROIDS FOR BLOOD CELL DEFICIENCIES

(57) **Abstract:** The present invention provides methods and compositions to prevent or treat a hematopoietic disorder such as thrombocytopenia or neutropenia by administering to a subject an effective amount of a steroid such as 3,7,16,17-tetrahydroxy-androst-5-ene, 3,16,17-trihydroxyandrostane, 3-hydroxy-16-haloandrostane-17-one or 3,17-dihydroxy-16-haloandrostane.

Inte ional Application No PCT/US 00/26771

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K31/565 A61K31/566 A61P7/06

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) $IPC \ 7 \qquad A61K$

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)

CHEM ABS Data, EPO-Internal, WPI Data, PAJ, EMBASE, SCISEARCH, BIOSIS, MEDLINE

C. DOCOM	ENTS CONSIDERED TO BE RELEVANT				
Category °	Citation of document, with indication, where appropriate, of	the relevant passages	Relevant to claim No.		
X	SINGER J W ET AL: "STEROIDS A HEMATOPOIESIS PART 1 THE EFFE STEROIDS ON IN-VITRO ERYTHROID GROWTH STRUCTURE ACTIVITY RELA JOURNAL OF CELLULAR PHYSIOLOG vol. 88, no. 2, 1976, pages 12 XP001015349 ISSN: 0021-9541 figure 1 page 132, column 1, paragraph page 132, column 2, paragraph page 130; examples 3,10; table page 131; examples 2,12,17; table	CT OF D COLONY ATIONSHIPS" Y, 27-134, 2 4	1-6, 8-10, 14-28, 30,31		
X	WO 97 13500 A (SUPERGEN INC) 17 April 1997 (1997-04-17)		1-6, 8-10, 12-31		
Υ	page 6, line 16 - line 24 		4,7,11		
		_/			
X Furti	her 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 filling 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 filling date but later than the priority date claimed 		or priority date and not in conflict with cited to understand the principle or the invention *X* document of particular relevance; the cannot be considered novel or cannot involve an inventive step when the do *Y* document of particular relevance; the cannot be considered to involve an in document is combined with one or moments, such combination being obvious in the art.	 "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 		
Date of the	actual completion of the international search	Date of mailing of the international sea	arch report		
1	5 August 2001	27/08/2001			
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 Bonzano, C			

2

Into ional Application No
PCT/US 00/26771

	PC1/US 00/26//1	
	Relevant to claim No.	
Chancil of document, with indication, where appropriate, or the following passages	TIGIOTAIN TO GIANTINO.	
WO 97 17992 A (SUPERGEN INC) 22 May 1997 (1997-05-22)	1-6, 8-10, 12-20, 22-31	
page 12, line 17 - line 24 page 18, paragraph 2	4,7,11	
US 4 602 008 A (KRSEK GEORGE) 22 July 1986 (1986-07-22)	1-6, 8-10, 12-20, 22-31	
page 1, paragraph 4 example 9 column 2, paragraph 2 - paragraph 4	4,7,11	
US 5 763 433 A (MORFIN ROBERT) 9 June 1998 (1998-06-09)	1-6, 8-10, 12-20, 22-31	
column 1, paragraph 5 - paragraph 6 column 5, line 50 - line 60 claim 7		
LAFAYE, PIERRE ET AL: "The 7.alphahydroxysteroids produced in human tonsils enhance the immune response to tetanus toxoid and Bordetella pertussis antigens" BIOCHIM. BIOPHYS. ACTA (1999), 1472(1-2), 222-231, XP001014347 page 229, column 1, paragraph 3 page 223, column 1, paragraph 1 page 230, column 1, paragraph 2 - paragraph 3	1-6, 8-10, 12-20, 22-31	
DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1983 FEDOROVSKAYA N A ET AL: "CHARACTERISTICS OF IMMUNO HEMATOLOGIC PARAMETERS IN PATIENTS WITH HYPOPLASTIC ANEMIA DURING REMISSION" Database accession no. PREV198477064932 XP002174053 abstract & GEMATOLOGIYA I TRANSFUZIOLOGIYA,	1-6, 8-10, 12-20, 22-31	
	page 12, line 17 - line 24 page 18, paragraph 2 US 4 602 008 A (KRSEK GEORGE) 22 July 1986 (1986-07-22) page 1, paragraph 4 example 9 column 2, paragraph 2 - paragraph 4 US 5 763 433 A (MORFIN ROBERT) 9 June 1998 (1998-06-09) column 1, paragraph 5 - paragraph 6 column 5, line 50 - line 60 claim 7 LAFAYE, PIERRE ET AL: "The 7.alphahydroxysteroids produced in human tonsils enhance the immune response to tetanus toxoid and Bordetella pertussis antigens" BIOCHIM. BIOPHYS. ACTA (1999), 1472(1-2), 222-231, XP001014347 page 229, column 1, paragraph 3 page 223, column 1, paragraph 1 page 230, column 1, paragraph 2 - paragraph 3 DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1983 FEDOROVSKAYA N A ET AL: "CHARACTERISTICS OF IMMUNO HEMATOLOGIC PARAMETERS IN PATIENTS WITH HYPOPLASTIC ANEMIA DURING REMISSION" Database accession no. PREV198477064932 XP002174053 abstract	

Into ional Application No
PCT/US 00/26771

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	<u> </u>
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	PIERELLI LUCA ET AL: "Erythropoietin addition to granulocyte colony-stimulating factor abrogates life-threatening neutropenia and increases peripheral-blood progenitor-cell mobilization after epirubicin, paclitaxel, and cisplatin combination chemotherapy: Results of a randomized comparison." JOURNAL OF CLINICAL ONCOLOGY, vol. 17, no. 4, April 1999 (1999-04), pages 1288-1295, XP001015368 ISSN: 0732-183X page 1292, column 2, paragraph 3 -page 1293, column 2, paragraph 1	4,7,11
Υ	ALONZI TONINO ET AL: "Interleukin-6 and CAAT/enhancer binding protein beta-deficient mice act as tools to dissect the IL-6 signalling pathway and IL-6 regulation." IMMUNOBIOLOGY, vol. 198, no. 1-3, December 1997 (1997-12), pages 144-156, XP001015352 ISSN: 0171-2985 page 153, line 3 - line 12	4,7,11

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-19,22-31 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed.

Present claim 12 relate to compounds defined by reference to a desirable characteristic or property, namely the activity as neutrophil or monocyte stimulator. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. Moreover, claims 1-9,12-15,18-22,30-31 relate to a therapeutic application which is actually not well defined.

In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds described in claims 20-21, optionally in association with the compounds mentioned in claims 4,7,11,13 in relation to the therapeutic applications defined in claims 10,16-17,23-24.

CLaims searched completely: 20-21. Claims searched incompletely: 1-18,22-31.

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.

Information on patent family members

inte ional Application No PCT/US 00/26771

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9713500	А	17-04-1997	CA 2208215 A CN 1173815 A EP 0801557 A HU 9801834 A JP 10508322 T	17-04-1997 18-02-1998 22-10-1997 01-02-1999 18-08-1998
WO 9717992	A	22-05-1997	US 5824668 A AU 718232 B AU 1158797 A CA 2237023 A CN 1201397 A EP 0866722 A	20-10-1998 13-04-2000 05-06-1997 22-05-1997 09-12-1998 30-09-1998
US 4602008	A	22-07-1986	NONE	
US 5763433	Α	09-06-1998	FR 2696934 A EP 0665752 A WO 9408588 A JP 8505124 T	22-04-1994 09-08-1995 28-04-1994 04-06-1996