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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 September 2004 (02.09.2004)

PCT

(10) International Publication Number
WO 2004/073728 A3

(51) International Patent Classification[7]: A61K 38/00, 38/17, 38/42, 39/02, A61P 35/00, 37/00

(21) International Application Number: PCT/EP2004/001553

(22) International Filing Date: 18 February 2004 (18.02.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
03003687.5 18 February 2003 (18.02.2003) EP

(71) Applicant: CLINIQUE LA PRAIRIE RESEARCH SA [LU/LU]; 5, Boulevard de la Foire, L-1528 Luxembourg (LU).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **WESTPHAL, Otto** [DE/CH]; Chemin de Ballallaz 18, CH-1820 Montreux (CH). **WÄLLI, Thierry** [CH/CH]; Clinique La Praire, CH-1815 Clarens-Montreaux (CH). **GORCZYNSKI, Reginald** [CA/CA]; Toronto Hospital, University of Toronto, 429 Drewry Avenue, Willowdale, Ontario M2R 2K6 (CA). **MÜLLER, Silke** [DE/DE]; Langenbrücken, Donauschwabenstr. 3A, 76669 Schönborn (DE). **MACH, Jean-Pierre** [CH/CH]; Institute of Biochemistry, University of Lausanne, CH-1011 Lausanne (CH). **HARTMANN, Alfred** [CH/CH]; Laubholzstr. 73, 8703 Erlenbach (CH). **BESSLER, Wolfgang** [DE/DE]; Inst. f. Mol. Med. u. Zellforschung; AG Tumorimmun, ol/ Vakzine, Albert-Ludwigs-Universität, Stefan-Meier-Str. 8, 79104 Freiburg (DE). **HOFMANN, Petra** [DE/DE]; Klinikum der Universität Regensburg; Abtteilung Hä, matologie und Internistische Onkologie, Franz-Josef-Strauss Allee 11, 93053 Regensburg (DE). **ZÄHRINGER, Ulrich** [DE/DE]; Forschungszentrum Borstel, Leibniz-Zentrum für Medizin und Blowissenschaften, Parkallee 22, 23845 Borstel (DE). **ALEXANDER, Christian** [DE/DE]; Forschungszentrum Borstel, Leibniz-Zentrum für Medizin und Blowissenschaften, Parkallee 22, 23845 Borstel (DE). **VOR DEM ESCHE, Ulrich** [DE/DE]; Almendweg 17, 79110 Freiburg (DE). **ULMER, Artur, J.** [DE/DE]; Forschungszentrum Borstel, Leibniz-Zentrum für Medizin und Blowissenschaften, Parkallee 22, 23845 Borstel (DE). **VERDINI, Antonio** [IT/IT]; Viale Marconi 29, I-47011 Castrocarro Terme (IT).

(74) Agent: **VOSSIUS & PARTNER**; Siebertstrasse 4, 81675 München (DE).

(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: 7 October 2004

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: COMPOSITIONS COMPRISING FETAL HEMOGLOBIN AND BACTERIAL ENDOTOXIN AND OPTIONALLY ADDITIONAL FETAL LIVER COMPONENTS

(57) Abstract: The present invention relates to a pharmaceutical composition representing a novel immunomodulating principle comprising bacterial endotoxin, fetal hemoglobin or more particularly a heme-free derivative or the γ-chain thereof, and optionally, components which are present in the fetal liver in addition to HbF. The composition is delivered to humans in a pharmaceutically acceptable carrier and/or diluent. In accordance with the present invention it was surprisingly found that endotoxin and fetal hemoglobin partial structures display a pronounced synergistic biomedical activity. The biomedical effect of fetal hemoglobin and its partial structures is surprisingly not based on a classical hemoglobin function as an oxygen transporter but related to a modulation of endotoxin-mediated bioactivity. This biomedical activity is surprisingly also observed after oral application of the composition. The composition of the invention finds a variety of applications which have in common the stimulation of the immune system and the reversion in polarization of cytokines and chemokines from a Th2-directed response to a Th1-type response. The proposed applications would therefore include the treatment of allergic conditions, malignancies, chronic infections, autoimmune phenomena and age-related imbalances.

WO 2004/073728 A3