



(51) International Patent Classification:

A61K 38/42 (2006.01) *A61K 47/30* (2006.01)
A61K 47/48 (2006.01) *A61P 35/00* (2006.01)

(21) International Application Number:

PCT/US2012/046130

(22) International Filing Date:

11 July 2012 (11.07.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

13/179,590 11 July 2011 (11.07.2011) US

(72) Inventors; and

(71) Applicants : **WONG, Bing Lou** [US/US]; 3592 S. Mall Street, Irvine, CA 92606 (US). **KWOK, Sui Yi** [CN/CN]; Flat 2907, 29/F, Pik Wai House, Shek Pai Wan Estate, Aberdeen, Hong Kong (CN). **LAU, Sze Hang** [CN/CN]; Block B, 3/F, 2 Lau Li Street, North Point, Hong Kong (CN).

(74) Agent: **YIP, Sam, T.**; Ella Cheong (Hong Kong) Limited, 5001 Hopewell Centre, 183 Queen's Road East, Wan Chai, Hong Kong (CN).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ,

CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))
- of inventorship (Rule 4.17(iv))

Published:

- without international search report and to be republished upon receipt of that report (Rule 48.2(g))

(54) Title: A HEAT STABLE OXYGEN CARRIER-CONTAINING PHARMACEUTICAL COMPOSITION FOR DIFFERENT TREATMENT APPLICATIONS

(57) Abstract: A highly purified and heat stable cross-linked nonpolymeric tetrameric hemoglobin suitable for use in mammals without causing renal injury and vasoconstriction is provided. A high temperature and short time (HTST) heat processing step is performed to remove undesired dimeric form of hemoglobin, uncross-linked tetrameric hemoglobin, and plasma protein impurities effectively. Addition of N-acetyl cysteine after heat treatment and optionally before heat treatment maintains a low level of met-hemoglobin. The heat stable cross-linked tetrameric hemoglobin can improve and prolong oxygenation in normal and hypoxic tissue. In another aspect, the product is used in the treatment of various types of cancer such as leukemia, colorectal cancer, lung cancer, breast cancer, liver cancer, nasopharyngeal carcinoma and esophageal cancer. The inventive tetrameric hemoglobin can also be used to prevent tumor metastasis and recurrence following surgical tumor excision. Further the inventive tetrameric hemoglobin can be administered to patients prior to chemotherapy and radiation treatment.

