



- (51) **International Patent Classification:**  
*A01N 35/00* (2006.01) *A61K 31/11* (2006.01)
- (21) **International Application Number:**  
PCT/US2012/072177
- (22) **International Filing Date:**  
28 December 2012 (28.12.2012)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**  
61/581,053 28 December 2011 (28.12.2011) US  
61/661,320 18 June 2012 (18.06.2012) US
- (71) **Applicants:** **GLOBAL BLOOD THERAPEUTICS, INC.** [US/US]; 29 Newbury Street, Boston, Massachusetts 02116 (US). **CYTOKINETICS, INC.** [US/US]; 280 East Grand Avenue, South San Francisco, California 94080 (US). **THE REGENTS OF THE UNIVERSITY OF CALIFORNIA** [US/US]; 1111 Franklin Street, 12th Floor, Oakland, California 94607 (US).
- (72) **Inventors:** **METCALF, Brian**; 297 Lakefield Place, Moraga, California 94556 (US). **CHUANG, Chihyuan**; 460 Bayview Ave., Millbrae, California 94030 (US). **WAR-RINGTON, Jeffrey**; 1936 Playa Street, San Mateo, California 94403 (US). **PAULVANNAN, Kumar**; 6974 Blue Hill Drive, San Jose, California 95129 (US). **JACOBSON, Matthew P.**; 370 Arkansas St., San Francisco, California 94107 (US). **HUA, Lan**; 2747 De Medio Ct., Apt 103B, Mountain View, California 94040 (US). **MORGAN, Bradley**; 120 Rimer Dr., Moraga, California 94556 (US).

(74) **Agents:** **HOPKINS, Mark** et al.; Kilpatrick Townsend & Stockton LLP, Two Embarcadero Center, Eighth Floor, San Francisco, California 94111-3834 (US).

(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, BN, 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, PA, 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).

**Published:**

— with international search report (Art. 21(3))

(54) **Title:** SUBSTITUTED BENZALDEHYDE COMPOUNDS AND METHODS FOR THEIR USE IN INCREASING TISSUE OXYGENATION

(57) **Abstract:** Provided are substituted benzaldehydes and derivatives thereof that act as allosteric modulators of hemoglobin, methods and intermediates for their preparation, pharmaceutical compositions comprising the modulators, and methods for their use in treating disorders mediated by hemoglobin and disorders that would benefit from increased tissue oxygenation.

