



(51) International Patent Classification:

A61K 31/197 (2006.01) C07C 229/34 (2006.01)
A61K 31/662 (2006.01) C07C 237/10 (2006.01)
C07C 271/46 (2006.01) C07C 237/30 (2006.01)
C07F 9/48 (2006.01) C07C 239/20 (2006.01)
C07C 309/66 (2006.01) A61P 35/00 (2006.01)
C07C 229/22 (2006.01)

(21) International Application Number:

PCT/US2015/014303

(22) International Filing Date:

3 February 2015 (03.02.2015)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/935,246 3 February 2014 (03.02.2014) US

(71) Applicant: **QUADRIGA BIOSCIENCES, INC.**
[US/US]; 1111 West El Camino Real, Suite 109-234,
Sunnyvale, CA 94087 (US).

(72) Inventors: **JANDELEIT, Bernd**; 1111 West El Camino
Real, Suite 109-234, Sunnyvale, CA 94087 (US). **FISC-
HER, Wolf-Nicolas**; 1111 West El Camino Real, Suite
109-234, Sunnyvale, CA 94087 (US). **KOLLER, Kerry,
J.**; 1111 West El Camino Real, Suite 109-234, Sunnyvale,
CA 94087 (US).

(74) Agents: **LAMBERT, William, R.** et al.; Kilpatrick Town-
send & Stockton LLP, Two Embarcadero Center, 8th
Floor, San Francisco, CA 94111 (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, IR, IS, JP, KE, KG, KN, KP, KR,
KZ, LA, LC, LK, LR, LS, 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, SA, 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, ST, 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, KM, ML, MR, NE, SN, TD, TG).

Published:

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

(54) Title: BETA-SUBSTITUTED BETA-AMINO ACIDS AND ANALOGS AS CHEMOTHERAPEUTIC AGENTS

(57) Abstract: β -Substituted β -amino acids, β -substituted β -amino acid derivatives, and β -substituted β -amino acid analogs and (bio)isosteres and their use as chemotherapeutic agents are disclosed. The β -substituted β -amino acid derivatives and β -substituted β -amino acid analogs and (bio)isosteres are selective LAT1/4F2hc substrates and exhibit rapid uptake and retention in tumors expressing the LAT1/4F2hc transporter. Methods of synthesizing the β -substituted β -amino acid derivatives and β -substituted β -amino acid analogs and methods of using the compounds for treating cancer are also disclosed. The β -substituted β -amino acid derivatives and β -substituted β -amino acid analogs exhibit selective uptake in tumor cells expressing the LAT1/4F2hc transporter and accumulate in cancerous cells when administered to a subject in vivo. The β -substituted β -amino acid derivatives and β -substituted β -amino acid analogs and (bio)isosteres exhibit cytotoxicity toward several tumor types.

