

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
23 November 2017 (23.11.2017)



(10) International Publication Number
WO 2017/201502 A1

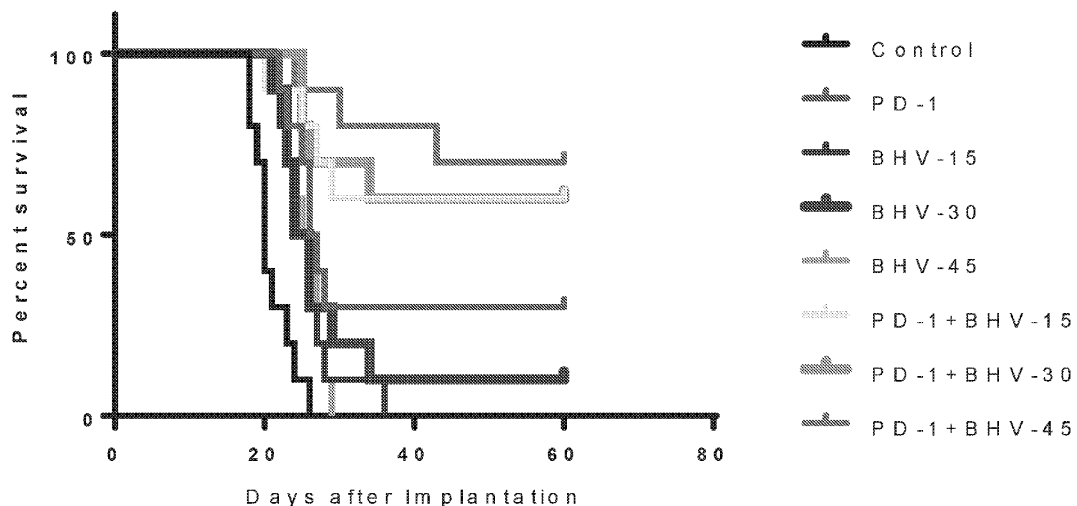
- (51) **International Patent Classification:**
A61K 31/428 (2006.01) *C07D 277/82* (2006.01)
- (21) **International Application Number:**
PCT/US2017/033690
- (22) **International Filing Date:**
19 May 2017 (19.05.2017)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
62/339,433 20 May 2016 (20.05.2016) US
- (71) **Applicant:** BIOHAVEN PHARMACEUTICAL
HOLDING COMPANY LTD. [US/US]; 234 Church
Street, Suite 301, New Haven, Connecticut 06520 (US).
- (72) **Inventor:** CORIC, Vladimir; 234 Church Street, Suite
301, New Haven, Connecticut 06520 (US).
- (74) **Agent:** VOLLES, Warren, K. et al.; IPRAUXUS LEGAL,
LLC, P.O. Box 689, 67 Sterling Hill Road, Old Lyme, Con-
necticut 06371 (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, DJ, 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, KH, KN, KP, KR,
KW, 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).

(54) **Title:** USE OF GLUTAMATE MODULATING AGENTS WITH IMMUNOTHERAPIES TO TREAT CANCER

Figure 1



(57) **Abstract:** Disclosed are methods of treating cancer using a combination of an immunotherapeutic agent, such as, for example, a PD-1, PD-L1 or CTLA-4 checkpoint inhibitor, and a glutamate modulating agent such as riluzole or trigriluzole. Pharmaceutical compositions and kits including the immunotherapeutic agents and glutamate modulating agents are also disclosed.

[Continued on next page]

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*
- *of inventorship (Rule 4.17(iv))*

Published:

- *with international search report (Art. 21(3))*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*