



- (51) **International Patent Classification:**
A61K 31/513 (2006.01) *A61P 35/00* (2006.01)
- (21) **International Application Number:**
PCT/US2022/045875
- (22) **International Filing Date:**
06 October 2022 (06.10.2022)
- (25) **Filing Language:** English
- (26) **Publication Language:** English
- (30) **Priority Data:**
63/252,970 06 October 2021 (06.10.2021) US
63/330,529 13 April 2022 (13.04.2022) US
- (71) **Applicants:** NAVIRE PHARMA, INC. [US/US]; 421 Kipling Street, Palo Alto, CA 94301 (US). BRIDGEBO SERVICES, INC. [US/US]; 421 Kipling Street, Palo Alto, CA 94301 (US).
- (72) **Inventors:** BELTRAN, Pedro; 421 Kipling Street, Palo Alto, CA 94301 (US). DAMBKOWSKI, Carl; 421 Kipling Street, Palo Alto, CA 94301 (US). LIM, Justin; 421 Kipling Street, Palo Alto, CA 94301 (US). SINKEVICIUS, Kerstin; 421 Kipling Street, Palo Alto, CA 94301 (US). WADE, Anna; 421 Kipling Street, Palo Alto, CA 94301 (US). WALLACE, Eli; 421 Kipling Street, Palo Alto, CA 94301 (US). WOOD, Lauren; 421 Kipling Street, Palo Alto, CA 94301 (US). VAN VEEN-HUYZEN, David; 421 Kipling Street, Palo Alto, CA 94301 (US). WEN, Susanna; 421 Kipling Street, Palo Alto, CA 94301 (US).
- (74) **Agent:** DONG, Yaohua; Mintz, Levin, Cohn, Ferris, Glovsky & Popeo, P.C, One Financial Center, Boston, MA 02111 (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, CV, CZ, DE, DJ, DK, DM,

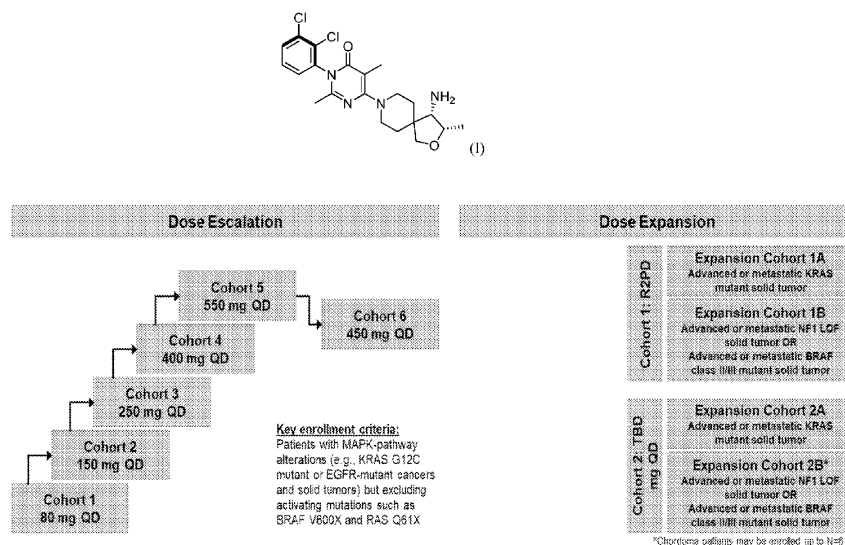
(54) **Title:** SUBSTITUTED PYRIMIDIN-4(3H)-ONES FOR USE IN TREATING CANCER

FIG. 14

(57) **Abstract:** The present disclosure provides a method of treating cancer or a solid tumor (e.g., an advanced or metastatic solid tumor) in a subject with a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt, hydrate, solvate, stereoisomer, conformational isomer, tautomer, or a combination thereof, where the subject has one or more mutations in the MAPK pathway and/or one or more mutations in *PTPN11*. In particular, the solid tumor is an advanced or metastatic KRAS mutant solid tumor (e.g., KRAS G12C-positive solid tumor); an advanced or metastatic NF1 loss-of-function (LOF) solid tumor or BRAF class II/III mutant solid tumor; or chordoma.

[Continued on next page]

DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, 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, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, 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, ME, 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))
- 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))