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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
17 November 2022 (17.11.2022)

WIPO | PCT

(10) International Publication Number
WO 2022/237720 A1

(51) International Patent Classification:
A61K 31/53 (2006.01) *A61P 35/02* (2006.01)

(21) International Application Number:
PCT/CN2022/091679

(22) International Filing Date:
09 May 2022 (09.05.2022)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PCT/CN2021/093036
11 May 2021 (11.05.2021) CN
PCT/CN2021/100523
17 June 2021 (17.06.2021) CN
PCT/CN2022/086004
11 April 2022 (11.04.2022) CN

(71) Applicant: **JANSSEN PHARMACEUTICA NV** [BE/BE]; Turnhoutseweg 30, 2340 Beerse (BE).

(71) Applicant *(for SC only)*: **JOHNSON & JOHNSON (CHINA) INVESTMENT LTD.** [CN/CN]; 2101, No.1 Building, 65 Gui Qing Road, Xuhui District, Shanghai 200233 (CN).

(72) Inventors: **DASKALAKIS, Nikki**; Janssen Research & Development, LLC, 920 US Route 202, PO Box 300, Raritan, New Jersey 08869 (US). **GUTTKE, Christina Diane**; Janssen Research & Development, LLC, 920 US Route 202, PO Box 300, Raritan, New Jersey 08869 (US). **KWON, Min Chul**; Janssen Pharmaceutica NV, Turnhoutseweg 30, 2340 Beerse (BE). **FERRANTE, Lucille Angela**; Janssen Research & Development, LLC, 920 US Route 202, PO Box 300, Raritan, New Jersey 08869 (US). **PACKMAN, Kathryn Elizabeth**; Janssen Research & Development, LLC, 920 US Route 202, PO Box 300, Raritan, New Jersey 08869 (US). **PIETSCH, Eva Christine**; Janssen Research & Development, LLC, 920 US Route 202, PO Box 300, Raritan, New Jersey 08869 (US). **PHILIPPAR, Ulrike**; Janssen Pharmaceutica NV, Turnhoutseweg 30, 2340 Beerse (BE). **VERHULST, Tinne Ann J**; Janssen Pharmaceutica NV, Turnhoutseweg 30, 2340 Beerse (BE). **BHOGAL, Balpreet**; Janssen Research & Development, LLC, 920 US Route 202, PO Box 300, Raritan, New Jersey 08869 (US). **SUN, Yu**; Janssen Research & Development, LLC, 920 US Route 202, PO Box 300, Raritan, New Jersey 08869 (US). **CAI, Wei**; Johnson & Johnson (China) Investment Ltd., 2101, No.1 Building, 65 Gui Qing Road, Xuhui District, Shanghai 200233 (CN). **DAI, Xuedong**; Johnson & Johnson (China) Investment Ltd., 2101, No.1 Building, 65 Gui Qing Road, Xuhui District, Shang-

(54) Title: COMBINATION THERAPIES

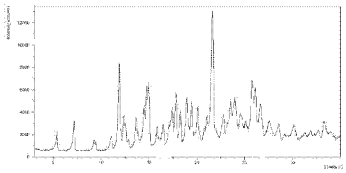
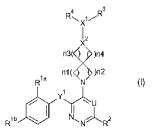


FIG. 1



(I)

(57) Abstract: Disclosed are combinations comprising a therapeutically effective amount of a menin-MLL inhibitor of Formula (I) or a pharmaceutically acceptable salt or a solvate thereof; and a therapeutically effective amount of a BCL-2 inhibitor; and optionally, a therapeutically effective amount of at least one other antineoplastic agent. Also disclosed are methods for treating a subject who has been diagnosed with a hematopoietic disorder using such combinations. Compounds are represented by Formula (I) as follows: wherein R^{1a}, R^{1b}, R^{2}, R^{3}, R^{4}, U, Y^{1}, X^{1}, X^{2}, n1, n2, n3 and n4 are defined herein.

[Continued on next page]

WO 2022/237720 A1

hai 200233 (CN). **QUEROLLE, Olivier Alexis Georges**; Janssen-Cilag, 1 Rue Camille Desmoulins, TSA 91003, 92787 Issy-les Moulineaux Cedex 9 (FR). **THURING, Johannes Wilhelmus J.**; Janssen Pharmaceutica NV, Turnhoutseweg 30, 2340 Beerse (BE). **LIU, Yingtao**; Johnson & Johnson (China) Investment Ltd., 2101, No.1 Building, 65 Gui Qing Road, Xuhui District, Shanghai 200233 (CN). **LIU, Lianzhu**; Johnson & Johnson (China) Investment Ltd., 2101, No.1 Building, 65 Gui Qing Road, Xuhui District, Shanghai 200233 (CN). **XU, Yanping**; Johnson & Johnson (China) Investment Ltd., 2101, No.1 Building, 65 Gui Qing Road, Xuhui District, Shanghai 200233 (CN). **FU, Liqiang**; Johnson & Johnson (China) Investment Ltd., 2101, No.1 Building, 65 Gui Qing Road, Xuhui District, Shanghai 200233 (CN). **LI, Ming**; Johnson & Johnson (China) Investment Ltd., 2101, No.1 Building, 65 Gui Qing Road, Xuhui District, Shanghai 200233 (CN). **FANG, Lichao**; Johnson & Johnson (China) Investment Ltd., 2101, No.1 Building, 65 Gui Qing Road, Xuhui District, Shanghai 200233 (CN). **DENG, Xiangjun**; Johnson & Johnson (China) Investment Ltd., 2101, No.1 Building, 65 Gui Qing Road, Xuhui District, Shanghai 200233 (CN). **NG, Alicia Tee Fuay**; Johnson & Johnson (China) Investment Ltd., 2101, No.1 Building, 65 Gui Qing Road, Xuhui District, Shanghai 200233 (CN). **DARVILLE, Nicolas Freddy J**; Janssen Pharmaceutica NV, Turnhoutseweg 30, 2340 Beerse (BE). **PANDE, Vineet**; Janssen Pharmaceutica NV, Turnhoutseweg 30, 2340 Beerse (BE).

(74) **Agent: NTD UNIVATION INTELLECTUAL PROPERTY AGENCY LTD.**; 10th Floor, Tower C, Beijing Global Trade Center, 36 North Third Ring Road East, Dongcheng District, Beijing 100013 (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, 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, IQ, IR, IS, IT, JM, JO, 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, 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, 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).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

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))*

— *with sequence listing part of description (Rule 5.2(a))*