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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
19 March 2015 (19.03.2015)

WIPO | PCT

(10) International Publication Number
WO 2015/036583 A2

(51) International Patent Classification:
A61K 31/4045 (2006.01)

(21) International Application Number:
PCT/EP2014/069575

(22) International Filing Date:
15 September 2014 (15.09.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/877,714 13 September 2013 (13.09.2013) US

(71) Applicants: **AMGEN INC.** [US/US]; One Amgen Center Drive, Thousand Oaks, California 91320 (US). **AMGEN RESEARCH (MUNICH) GMBH** [DE/DE]; Staffelseestr. 2, 81477 Munich (DE).

(72) Inventors: **WALTER, Roland B.**; 1012 NE 95th Street, Seattle, Washington 98115-2218 (US). **SUBKLEWE, Marion**; Klinikum der Universitaet Muenchen, Med. Klinik III, Marchioninistrasse 15, 81377 Munich (DE). **KRUPKA, Christina**; Medizinische Klinik 3 am Klinikum Grosshadern Muenchen, Marchioninistrasse 15, 81377 Munich (DE).

(74) Agents: **KOCH, Andreas** et al.; Schiweck Weinzierl Koch, European Patent Attorneys, Landsberger Str. 98, 80339 Munich (DE).

(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:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

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

WO 2015/036583 A2

(54) Title: COMBINATION OF EPIGENETIC FACTORS AND BISPECIFIC COMPOUNDS TARGETING CD33 AND CD3 IN THE TREATMENT OF MYELOID LEUKEMIA

(57) Abstract: The present invention provides a combination epigenetic factors and bispecific compounds targeting CD33 and CD3 in the treatment of myeloid leukemia, wherein the epigenetic factor is selected from the group consisting of histone deacetylase (HDAC) inhibitors, DNA methyltransferase (DNMT) I inhibitors,hydroxyurea, Granulocyte-Colony Stimulating Factor (G-CSF), histone demethylase inhibitors and ATRA (All Trans-retinoic acid). Accordingly, the invention provides a pharmaceutical composition comprising a CD33 targeting compound and at least one epigenetic factor and an epigenetic factor for use in the amelioration and/or treatment of a myeloid leukemia, wherein the epigenetic factor increases the responsiveness of a patient to a CD33 targeting compound. Moreover, the invention provides the use of at least one an epigenetic factor for increasing the responsiveness of a myeloid leukemia patient to a treatment with a CD33 targeting compound, a method for the treatment of a myeloid leukemia, the method comprising the administration of at least one epigenetic factor and a CD33 targeting compound to a patient in the need thereof and a kit comprising a pharmaceutical composition of the invention or an epigenetic factor of the invention and a bispecific CD33 targeting compound.