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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
18 September 2025 (18.09.2025)

WIPO | PCT

(10) International Publication Number
WO 2025/194054 A1

(51) International Patent Classification:
C07D 491/22 (2006.01) *A61P 35/00* (2006.01)
C07D 519/00 (2006.01) *A61K 31/529* (2006.01)

(21) International Application Number:
PCT/US2025/019960

(22) International Filing Date:
14 March 2025 (14.03.2025)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/565,476 14 March 2024 (14.03.2024) US
63/645,612 10 May 2024 (10.05.2024) US

(71) Applicant: **AMGEN INC.** [US/US]; One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US).

(72) Inventors: **WURZ, Ryan Paul**; c/o Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US). **CHEN, Ning**; c/o Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US). **BAUER, Adriano**; c/o Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US). **EMMETIERE, Fabien**; c/o Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US). **AMEGADZIE, Albert K.**; c/o Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US). **WU, Zhichen**; c/o Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US). **WIGMAN, Benjamin**; c/o Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US). **ALLEN, John Gordon**; c/o Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US). **GREENMAN, Kevin Lloyd**; c/o Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US). **PETTUS, Liping H.**; c/o Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US). **ZHAO, Wei**; c/o Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US). **LANMAN, Brian Alan**; c/o Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US). **BOOKER, Shon**; c/o Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US). **JACKSON, Jeffrey**; c/o Amgen Inc., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US).

(74) Agent: **KORAKAS, Peter**; Amgen INC., One Amgen Center Drive, Thousand Oaks, California 91320-1799 (US).

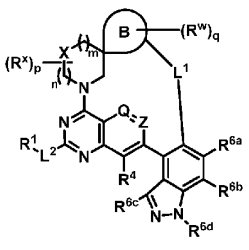
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, 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, MU, 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, UY, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, 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).

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))*

Published:
— *with international search report (Art. 21(3))*

(54) Title: SPIROCYCLIC COMPOUNDS AS MODULATORS OF KRAS AND USES THEREOF



(I)

(57) Abstract: Disclosed herein are compounds useful for the inhibition of KRAS G12D, G12V, G12A, G12S, G12R, G13D, Q61H, Q61L, Q61R or G12C. The compounds have a general Formula (I): (I) or pharmaceutically acceptable salts thereof, wherein the variables of Formula (I) are as defined herein. Also provided herein are pharmaceutical compositions comprising the compounds, uses of the compounds, and compositions for treatment of, for example, a KRAS G12D, G12V, G12A, G12S, G12R, G13D, Q61H, Q61L, Q61R or G12C disorder.

WO 2025/194054 A1