

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
19 September 2024 (19.09.2024)



(10) International Publication Number
WO 2024/189597 A1

(51) International Patent Classification:

C07D 498/18 (2006.01) *A61P 19/08* (2006.01)
A61P 3/04 (2006.01) *A61P 25/00* (2006.01)
A61P 3/08 (2006.01) *A61P 25/28* (2006.01)
A61P 9/04 (2006.01) *A61K 31/439* (2006.01)

(21) International Application Number:

PCT/IB2024/052545

(22) International Filing Date:

15 March 2024 (15.03.2024)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

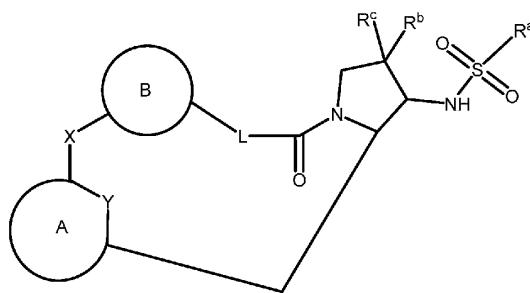
63/490,748 16 March 2023 (16.03.2023) US

(71) Applicant: **TAKEDA PHARMACEUTICAL COMPANY LIMITED** [JP/JP]; 1-1, Doshomachi 4-chome, Chuoku, Osaka-shi, Osaka 541-0045 (JP).

(72) Inventors: **KONO, Mitsunori**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **SASAKI, Yusuke**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **OGURO, Yuya**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **IKEDA, Zenichi**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **KUBO, Osamu**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **SETO, Masaki**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **YAMASHITA,**

Toru; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **KAMATA, Makoto**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **SATO, Kenjiro**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **REYNOLDS, Matthew Thomas**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **TAKAMI, Kazuaki**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **KI-NA, Asato**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **YUKAWA, Takafumi**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **NAKAMURA, Minoru**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **KAMEI, Taku**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **KAKEI, Hiroyuki**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **YAMAGUCHI, Fumie**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **OHASHI, Tomohiro**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **KAKEGAWA, Keiko**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **KOJI-**

(54) Title: MACROCYCLIC HETEROCYCLE COMPOUNDS AND USE THEREOF



(I)

(57) Abstract: The present invention provides a heterocyclic compound having an orexin type 2 receptor agonist activity. A compound represented by the formula (I): wherein each symbol is as described in the specification, or a salt thereof has an orexin type 2 receptor agonist activity, and is useful as an agent for the prophylaxis or treatment of narcolepsy.

[Continued on next page]

WO 2024/189597 A1

MA, Takuto; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **PÜNNER, Florian**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **MURAKAMI, Masataka**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **TANIGUCHI, Takahiko**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **KOIKE, Tatsuki**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **KAJITA, Yuichi**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **MIYANO HANA, Yuhei**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **TAKEUCHI, Kohei**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **ITO, Yoshiteru**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **TOKUNAGA, Norihito**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **HATTORI, Yasushi**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **KIMURA, Eiji**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **PAWLICZEK, Martin Alexander**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **PIRA, Marilena**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **IKEDA, Shuhei**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **TEZUKA, Noriyuki**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **WATANABE, Yoshikazu**; c/o TAKEDA PHARMACEUTICAL COMPANY LIMITED, 26-1, Muraoka-Higashi 2-chome, Fujisawa-shi, Kanagawa 251-0012 (JP). **CURRAN, Kevin**; c/o TAKEDA DEVELOPMENT CENTER AMERICAS, INC., 9625 Towne Centre Drive, San Diego, California 92121 (US). **DOERING, Nicole**; c/o TAKEDA DEVELOPMENT CENTER AMERICAS, INC., 9625 Towne Centre Drive, San Diego, California 92121 (US). **HOPKINS, Maria**; c/o TAKEDA DEVELOPMENT CENTER AMERICAS, INC., 9625 Towne Centre Drive, San Diego, California 92121 (US). **JOHNSON, Ben**; c/o TAKEDA DEVELOPMENT CENTER AMERICAS, INC., 9625 Towne Centre Drive, San Diego, California 92121 (US). **KIRYANOV, Andre**; c/o TAKEDA DEVELOPMENT CENTER AMERICAS, INC., 9625 Towne Centre Drive, San Diego, California 92121 (US). **LAM, Jon**; c/o TAKEDA DEVELOPMENT CENTER AMERICAS, INC., 9625 Towne Centre Drive, San Diego, California 92121 (US). **MURPHY, Sean**; c/o TAKE-

DA DEVELOPMENT CENTER AMERICAS, INC., 9625 Towne Centre Drive, San Diego, California 92121 (US). **O'ROURKE, Natasha**; c/o TAKEDA DEVELOPMENT CENTER AMERICAS, INC., 9625 Towne Centre Drive, San Diego, California 92121 (US). **REICHARD, Holly**; c/o TAKEDA DEVELOPMENT CENTER AMERICAS, INC., 9625 Towne Centre Drive, San Diego, California 92121 (US). **TANIS, Paul**; c/o TAKEDA DEVELOPMENT CENTER AMERICAS, INC., 9625 Towne Centre Drive, San Diego, California 92121 (US). **ZHANG, Yunlong**; c/o TAKEDA DEVELOPMENT CENTER AMERICAS, INC., 9625 Towne Centre Drive, San Diego, California 92121 (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, 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).

Published:

- with international search report (Art. 21(3))
- in black and white; the international application as filed contained color or greyscale and is available for download from PATENTSCOPE