

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
20 February 2025 (20.02.2025)



(10) International Publication Number
WO 2025/035212 A1

(51) International Patent Classification:

C07J 43/00 (2006.01) *A61P 5/32* (2006.01)
A61K 31/565 (2006.01) *A61P 35/00* (2006.01)
A61K 31/566 (2006.01) *C07J 41/00* (2006.01)

(21) International Application Number:

PCT/CA2024/051059

(22) International Filing Date:

14 August 2024 (14.08.2024)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

63/519,779 15 August 2023 (15.08.2023) US

(71) Applicant: UNIVERSITÉ LAVAL [CA/CA]; 2325 rue de l'Université, Québec, Québec G1V 0A6 (CA).

(72) Inventors: MALTAIS, René; 3070 Amarantes, Québec, Québec G1M 3Z7 (CA). POIRIER, Donald; 1588 des Cas-sandres, L'ancienne-Lorette, Québec G2E 5V1 (CA).

(74) Agent: CALVET, Damien et al.; Gowling WLG (Canada) LLP, 3700-1 Place Ville Marie, Montréal, Québec H3B 3P4 (CA).

(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).

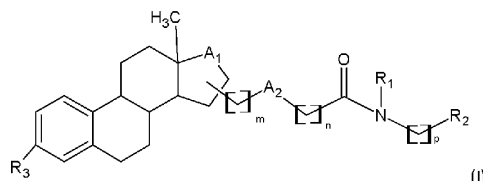
Declarations under Rule 4.17:

— 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))
— in black and white; the international application as filed contained color or greyscale and is available for download from PATENTSCOPE

(54) Title: IRREVERSIBLE 17BETA-HSD1 INHIBITORS



(57) Abstract: Compounds of formula (I), pharmaceutical compositions thereof, and kits thereof, are disclosed wherein A₁ is C(O) or CHR_{Z1} with R_{Z1} being OH, amine, imine, halogen, (C₁-C₅)alkoxy, OC(O)(C₁-C₅)alkyl, or OSO₂-amine; A₂ is CH₂ or O; R₁ is hydrogen, (C₁-C₅)alkyl optionally substituted with one or more Z substituents, (C₁-C₅)alkoxy optionally substituted with one or more Z substituents, (C₂-C₅)alkenyl optionally substituted with one or more Z substituents, (C₂-C₅)alkynyl optionally substituted with one or more Z substituents, (C₃-C₈)cycloalkyl, aryl, or heteroaryl; Z is halogen, OH, (C₁-C₅)alkyl, (C₁-C₅)haloalkyl, (C₁-C₅)alkoxy, (C₁-C₅)haloalkoxy, or amine; R₂ is a heterocyclic aromatic ring having 5, 6 or 7 members having at least one N, S and/or O; R₃ is a (C₁-C₅)alkyl substituted with one or more Br, Br⁷⁶, I, I¹²³, I¹²⁴, or I¹³¹; m is an integer from 0 to 2; n is an integer from 0 to 2; and p is an integer from 0 to 5. Compounds of Formula I are inhibitors of 17β-Hydroxysteroid dehydrogenase type 1 (17β-HSD1) and are for use in the treatment or prevention of steroid hormone dependent disease, such as breast cancer, lung cancer, prostate carcinoma, ovarian cancer, uterine cancer, endometrial cancer and endometrial hyperplasia.

WO 2025/035212 A1