

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
15 February 2024 (15.02.2024)



(10) International Publication Number
WO 2024/033278 A1

(51) International Patent Classification:

C07K 5/09 (2006.01) A61P 31/04 (2006.01)
A61K 38/06 (2006.01)

(21) International Application Number:

PCT/EP2023/071759

(22) International Filing Date:

07 August 2023 (07.08.2023)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

22189412.4 09 August 2022 (09.08.2022) EP

(71) Applicant (for all designated States except US): **F. HOFFMANN-LA ROCHE AG** [CH/CH]; Grenzacherstrasse 124, 4070 Basel (CH).

(71) Applicant (for US only): **HOFFMANN-LA ROCHE INC.** [US/US]; Overlook at Great Notch, 150 Clove Road, 8th Floor, Suite 8 - Legal Department, Little Falls, New Jersey 07424 (US).

(72) Inventors: **BIGLER, Raphael**; c/o F. Hoffmann-La Roche AG, Grenzacherstrasse 124, 4070 Basel (CH). **BLISS, Fritz Theodor**; c/o F. Hoffmann-La Roche AG, Grenzacherstrasse 124, 4070 Basel (CH). **FANTASIA, Serena Maria**; c/o F. Hoffmann-La Roche AG, Grenzacherstrasse 124, 4070 Basel (CH). **HOFFMANN-EMERY, Fabienne Roxane**; c/o F. Hoffmann-La Roche AG, Grenzacherstrasse 124, 4070 Basel (CH). **SANTANDREA, Ernesto**; c/o F. Hoffmann-La Roche AG, Grenzacherstrasse 124, 4070 Basel (CH).

(74) Agent: **NEUHAUS, Christian**; c/o F. Hoffmann-La Roche AG, Patent Department, Grenzacherstrasse 124, 4070 Basel (CH).

(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,

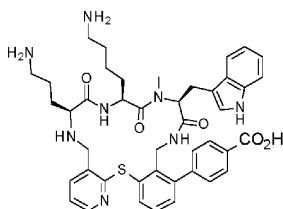
KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(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))

(54) Title: PROCESS FOR MANUFACTURING AN ANTIBIOTIC MACROCYCLIC PEPTIDE



(I)

(57) Abstract: The invention relates to a novel process for manufacturing 4-[(11S,14S,17S)-14-(4-Aminobutyl)-11-(3-aminopropyl)-17-(1H-indol-3-ylmethyl)-16-methyl-12,15,18-trioxo-2-thia-4,10,13,16,19-pentazatricyclo[19.4.0.0.3,8]pentacosal-1(25),3(8),4,6,21,23-hexaen-22-yl]benzoic acid (I), or a pharmaceutically acceptable salt thereof. The invention further relates to certain synthetic intermediates that are useful for the novel process according to the invention. The process according to the invention is particularly suitable for large-scale manufacturing of the compound of formula (I) under GMP conditions.

WO 2024/033278 A1