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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
23 June 2016 (23.06.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/096843 A1

(51) **International Patent Classification**:
A61K 51/10 (2006.01) *A61P 35/00* (2006.01)

(21) **International Application Number**:
PCT/EP2015/079773

(22) **International Filing Date**:
15 December 2015 (15.12.2015)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:
1422512.2 17 December 2014 (17.12.2014) GB

(71) **Applicant**: **BAYER AS** [NO/NO]; Drammensveien 147, 0277 Oslo (NO).

(72) **Inventor**: **CUTHBERTSON, Alan**; Bayer AS, Drammensveien 147, 0277 Oslo (NO).

(74) **Agent**: **BIP PATENTS**; c/o Bayer Intellectual Property GmbH, Alfred-Nobel-Str. 10, 40789 Monheim am Rhein (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).

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))*

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

WO 2016/096843 A1

(54) **Title**: RADIO-PHARMACEUTICAL COMPLEXES

(57) **Abstract**: The invention provides a method for the formation of a tissue-targeting thorium complex, said method comprising; a) forming an octadentate chelator comprising four hydroxypyridinone (HOPO) moieties, substituted in the N-position with a C_{1}-C_{3} alkyl group, and a coupling moiety terminating in a carboxylic acid group; b) coupling said octadentate chelator to at least one tissue-targeting peptide or protein comprising at least one amine moiety by means of at least one amide-coupling reagent whereby to generate a tissue-targeting chelator; and c) contacting said tissue-targeting chelator with an aqueous solution comprising an ion of at least one alpha-emitting thorium isotope. A method of treatment of a neoplastic or hyperplastic disease comprising administration of such a tissue-targeting thorium complex, as well as the complex and corresponding pharmaceutical formulations are also provided.