

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

(19) World Intellectual Property
Organization

International Bureau

(43) International Publication Date
14 March 2019 (14.03.2019)



(10) International Publication Number
WO 2019/051269 A1

(51) International Patent Classification:

A61K 31/519 (2006.01) *A61P 35/00* (2006.01)

C07D 471/00 (2006.01)

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).

(21) International Application Number:

PCT/US2018/050018

(22) International Filing Date:

07 September 2018 (07.09.2018)

Published:

- with international search report (Art. 21(3))
- with sequence listing part of description (Rule 5.2(a))

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/556,117 08 September 2017 (08.09.2017) US

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(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, DJ, DK, DM, DO,
DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN,
HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP,
KR, KW, 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,



WO 2019/051269 A1

(54) Title: ENPP1 INHIBITORS AND THEIR USE FOR THE TREATMENT OF CANCER

(57) Abstract: Compounds, compositions and methods are provided for the inhibition of ENPP1. Aspects of the subject methods include contacting a sample with a ENPP1 inhibitor to inhibit cGAMP hydrolysis activity of ENPP1. In some cases, the ENPP1 inhibitor is cell impermeable. Also provided are compositions and methods for treating cancer. Aspects of the methods include administering to a subject a therapeutically effective amount of a ENPP1 inhibitor to treat the subject for cancer. In certain cases, the cancer is a solid tumor cancer. Also provided are methods of administering radiation therapy to a subject either before or after administering an ENPP1 inhibitor. The radiation therapy can be administered at a dosage and/or frequency effective to reduce radiation damage to the subject. In certain cases, the method is performed in combination with a chemotherapeutic agent, or a checkpoint inhibitor, or both.