

Product Data Sheet

Product Name: APG-115

Cat. No.: GC35367

Chemical Properties

Cas. No. 1818393-16-6

SMILES O=C1NC2=CC(Cl)=CC=C2[C@]13C4(CCCCC4)N(CC)[C@@H](C(NC56CCC(CC6)(C(O)=O)CC5)=O)[C@@H]3C7=C(C(Cl)=CC=C7)F

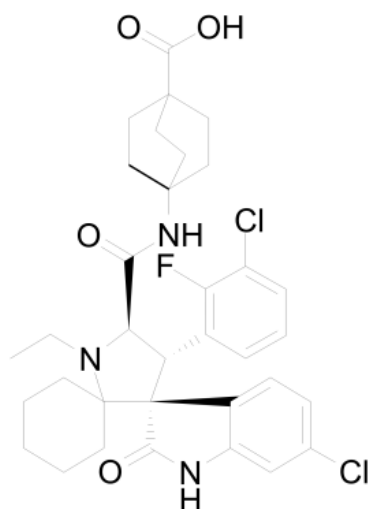
Formula $C_{34}H_{38}Cl_2FN_3O_4$ M.Wt 642.59

Solubility Soluble in DMSO Storage Store at -20°C

General tips For obtaining a higher solubility, please warm the tube at 37 °C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT, or blue ice upon request.

Structure



Background

APG-115 (AA-115) is an orally active MDM2 protein inhibitor binding to MDM2 protein with IC₅₀ and K_i values of 3.8 nM and 1 nM, respectively[1]. APG-115 blocks the interaction of MDM2 and p53 and induces cell-cycle arrest and apoptosis in a p53-dependent manner[2][3]. IC₅₀: 3.8 nM (APG-115)[1]

APG-115 (0.001-100 μM; 72 hours) inhibits cell proliferation in concentration-dependent manner, with IC₅₀s of 18.9 ± 15.6 nM and 103.5 ± 18.3 nM respectively in AGS and MKN45 cells[3]. APG-115

Caution: Product has not been fully validated for medical applications. For research use only.

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(0.02 μ M, 0.2 μ M; 48 hours) enhances the anti-proliferative effect of radiotherapy at different radiation dose[3]. APG-115 (0.02 μ M, 0.2 μ M; 48 hours) affects progression by inducing cells arrested at G0/G1 phase in AGS and MKN45 cell with wild p53[3]. APG-115 (0.02 μ M, 0.2 μ M; 24 hours) activates p53 to enhance radiosensitivity in AGS and MKN45 cells; stable knockout of p53 abrogates expression of MDM2, p53, p21, PUMA, BAX, Cleaved-caspase3, γ H2AX[3]. APG-115 (0.3 μ M, 1 μ M, 3 μ M, 10 μ M; 24 hours) leads to a concentration-dependent cell cycle arrest in G2/M phases and a decreasing in S-phase in p53 wide-type cell lines (TPC-1, KTC-1)[4]. Cell Proliferation Assay[3] Cell Line: AGS and MKN45 cells

APG-115 (Delivered orally; 100 mg/kg; once daily; 10 days) enhances radiation antitumor effect in gastric adenocarcinoma in vivo[3]. Animal Model: Four-week-old male BALB/c athymic nude mice with MKN45 cells[3]

[1]. Angelo Aguilar, et al. 4-((3'R,4'S,5'R)-6''-Chloro-4'-(3-chloro-2-fluorophenyl)-1'-ethyl-2''-oxodispiro[cyclohexane-1,2'-pyrrolidine-3',3''-indoline]-5'-carboxamido)bicyclo[2.2.2]octane-1-carboxylic Acid (AA-115/APG-115): A Potent and Orally Active Murine Double Minute 2 (MDM2) Inhibitor in Clinical Development. J Med Chem. 2017 Apr 13; 60(7): 2819-2839. [2]. A W Tolcher et al, A phase Ib/II study of APG-115 in combination with pembrolizumab in patients with unresectable or metastatic melanomas or advanced solid tumors, Ann Oncol. 2019 Feb 1; 30(Supplement_1). pii: mdz027. [3]. Hanjie Yi et al, A novel small molecule inhibitor of MDM2-p53 (APG-115) enhances radiosensitivity of gastric adenocarcinoma, J Exp Clin Cancer Res. 2018 May 2;37(1):97. [4]. Chen H, et al. Restoration of p53 using the novel MDM2-p53 antagonist APG115 suppresses dedifferentiated papillary thyroid cancer cells. Oncotarget. 2017 Jun 27;8(26):43008-43022.

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