Product Name: RG7388

Revision Date: 6/30/2016

Product Data Sheet

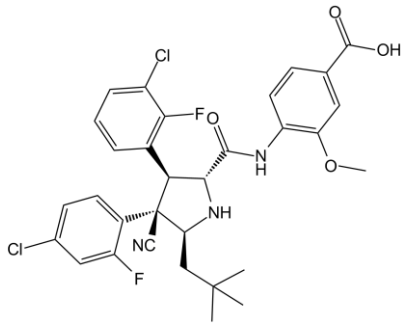
Chemical Properties

Product Name: RG7388

Cas No.: 1229705-06-9

M.Wt: 616.48

Formula: C31H29Cl2F2N3O4



Synonyms: RG 7388;RG-7388

Chemical Name: 4-[[(2R,3S,4R,5S)-3-(3-chloro-2-fluorophenyl)-4-(4-chloro-2-fluorophenyl)-4-cyano-5-(2,2-dimethylpropyl)pyrrolidine-2-carbonyl]amino]-3-methoxybenzoic acid

Canonical SMILES: CC(C)(C)CC1C(C(C(N1)C(=O)NC2=C(C=C(C=C2)C(=O)O)OC)C3=C(C(=CC=C3)Cl)F)(C#N)C4=C(C=C(C=C4)Cl)F

Solubility: >30.8mg/mL 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.

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

Biological Activity

Targets : p53

Pathways: Apoptosis >> p53

Description:

RG7388 is a second generation clinical MDM2 inhibitor with superior potency and selectivity. It is a highly potent pyrrolidine compound. RG7388 is more potent and selective than RG7112. In human cancer cell lines, IC50 value of RG7388 in HTRF binding assays is 6 nM and IC50 value of RG7388 in MTT proliferation assays is 0.03μM. [1]

In human cancer cell lines, RG7388 blocks p53−MDM2 binding and effectively activates the p53 pathway, leading to cell cycle arrest and/or apoptosis in cell lines expressing wild-type p53 and tumor growth inhibition or regression of osteosarcoma xenografts in nude mice. RG7388 is undergoing clinical investigation in solid and hematological tumors. [1]
In rhabdomyosarcoma xenografts mice, RG7388 increased the activity of Ionizing radiation (XRT) in both rhabdomyosarcoma models and did not increasing local XRT-induced skin toxicity. Changes in TP53-responsive genes were consistent with the synergistic activity of RG7388 and XRT in the Rh18 model. [2]
RG7388 GI50 concentrations of wt p53 was a >200-fold difference versus mutant cell lines. Comparing with MYCN- cells, Tet21N MYCN+ cells were more sensitive to RG7388. In five p53-wt neuroblastoma cell lines, combining use of RG7388 with cisplatin, topotecan, doxorubicin, busulfan and temozolomide were synergistic led to increased apoptosis and higher caspase-3/7 activity. RG7388 is highly potent against p53-wt neuroblastoma cells, and strongly supports its further evaluation as a novel therapy for patients with high-risk neuroblastoma and wt p53 to potentially improve survival and/or reduce toxicity. [3]

***Reference**:*
1.Ding Q, Zhang Z, Liu JJ et al. Discovery of RG7388, a potent and selective p53-MDM2 inhibitor in clinical development. J Med Chem. 2013 Jul 25;56(14):5979-83.
2.Phelps D, Bondra K, Seum S et al. Inhibition of MDM2 by RG7388 confers hypersensitivity to X-radiation in xenograft models of childhood sarcoma. Pediatr Blood Cancer. 2015 Apr 1. doi: 10.1002/pbc.25465.
3.Chen L, Rousseau RF, Middleton SA et al. Pre-clinical evaluation of the MDM2-p53 antagonist RG7388 alone and in combination with chemotherapy in neuroblastoma. Oncotarget. 2015 Apr 30;6(12):10207-21.

Protocol

Cell experiment:

Cell lines	Wild-type (wt)-p53 cancer cell lines (SJSA1, RKO, HCT116)
Preparation method	The solubility of this compound in DMSO is >10 mM. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.
Reacting conditions	~ 10 μM; 24 hrs
Applications	In cancer cells expressing wt-p53, RG7388 inhibited cell proliferation with an IC50 value of 30 nM, and induced dose-dependent p53 stabilization, cell cycle arrest, as well as cell apoptosis.

Animal experiment [3]:

Animal models	Mice bearing SJSA1 human osteosarcoma xenografts
Dosage form	25 or 50 mg/kg; p.o.; q.d., for 32 days
Applications	In a mouse SJSA1 human osteosarcoma xenograft model, RG7388 (25 mg/kg, p.o.) caused tumor growth inhibition and regression.
Other notes	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

***Reference**:*
[1]. Ding Q, Zhang Z, Liu JJ et al. Discovery of RG7388, a potent and selective p53-MDM2 inhibitor in clinical development. J Med Chem. 2013 Jul 25;56(14):5979-83.

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

ApexBio Technology

www.apexbt.com

7505 Fannin street, Suite 410, Houston, TX 77054.

Tel: +1-832-696-8203 | Fax: +1-832-641-3177 | Email: info@apexbt.com