

Product Data Sheet

Product Name: RG7388
Cat. No.: GC11594

Chemical Properties

Cas. No. 1229705-06-9

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

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

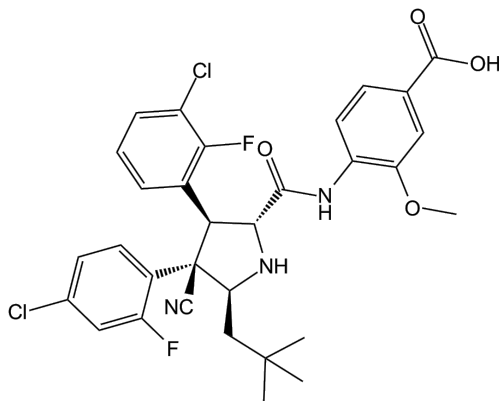
Formula $C_{31}H_{29}Cl_2F_2N_3O_4$ M.Wt 616.48

Solubility ≥ 30.824 mg/mL in DMSO, ≥ 6.96 mg/mL in EtOH with gentle warming 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



Protocol

Cell experiment [1]:

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Cell lines	MOLT-3 cells (human T-cell acute lymphoblastic leukemia cell line) and patient-derived xenograft (PDX) T-ALL cells
Preparation Method	MOLT-3 cells were maintained in RPMI-1640 medium supplemented with 10% heat-inactivated fetal bovine serum (FBS) at 37°C, 5% CO ₂ . Isogenic control and TP53 knockout MOLT-3 cells were treated with RG7388 at concentrations of 30–90nM for 24–72hours.
Reaction Conditions	30–90nM; 24-72 hours.
Applications	RG7388 significantly induced p53 protein stabilization and accumulation in TP53-wildtype MOLT-3 cells, leading to upregulation of pro-apoptotic genes BAX and BBC3 (PUMA) at RNA and protein levels. RG7388 treatment resulted in increased caspase-3/7 activity and apoptosis in a p53-dependent manner.

Animal experiment [2]:

Animal models	Th-ALKF1174L/MYCN genetically engineered mouse model (GEMM) and patient-derived xenograft (PDX) models (GR-NB4, IC-pPDX-112, HSJD-NB-012)
Preparation Method	Tumor-bearing mice were treated with RG7388 orally at 40-75mg/kg daily on a 5-days-on/2-days-off schedule for 14-21 days, either alone or in combination with Lorlatinib (10mg/kg). Tumor volume was monitored by MRI or caliper measurements.

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Dosage form 40-75mg/kg; oral gavage; Daily administration (5 days/week for 2-3 weeks).

Applications RG7388 monotherapy showed modest tumor growth inhibition in 3 of 4 PDX models, with complete resistance observed in an ETP-ALL model. However, RG7388 combined with Lorlatinib resulted in complete tumor regression in ALK-amplified GR-NB4 PDX models and significantly delayed tumor regrowth across multiple neuroblastoma models.

References:

[1] Johansson KB, Zimmerman MS, Dmytrenko IV, et al. Idasanutlin and navitoclax induce synergistic apoptotic cell death in T-cell acute lymphoblastic leukemia. *Leukemia*. 2023 Dec;37(12):2356-2366.

[2] Tucker ER, Jiménez I, Chen L, et al. Combination Therapies Targeting ALK-aberrant Neuroblastoma in Preclinical Models. *Clin Cancer Res*. 2023 Apr 3;29(7):1317-1331.

Background

RG7388 is an orally active MDM2 antagonist ($IC_{50}=6nM$) that activates the p53 pathway by inhibiting the MDM2-p53 interaction^[1-2]. RG7388 can induce cell cycle arrest to reduce tumor cell proliferation and is applicable for research related to acute myeloid leukemia and solid tumors^[3-4].

In vitro, treatment of TP53 wild-type T-cell acute lymphoblastic leukemia (T-ALL) cell line MOLT-3 with RG7388 (0-90nM) for 24-72 hours, RG7388 induced p53-dependent stabilization and accumulation of p53 protein, upregulated the expression of the pro-apoptotic BH3 domain genes BAX and BBC3 (PUMA), and increased caspase-3/7 activity and apoptosis^[5]. Treatment of colorectal cancer (CRC) cell lines HCT116 and RKO with RG7388 (1 μ M) for 24 hours, RG7388 induced p53 protein accumulation. In combination with the HSP90 inhibitor Ganetespib (50nM), RG7388 synergistically reduced cell viability and confluence, and increased cell death and PARP-1 cleavage^[6].

In vivo, oral co-administration of RG7388 (40-75mg/kg) with the ALK inhibitor Lorlatinib (10mg/kg) in

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ALK-amplified neuroblastoma PDX model (GR-NB4) mice (5 times per week for 2-3 weeks) leads to complete tumor regression. The combination therapy enhances apoptotic effects in vivo by activating the p53-BAX pathway^[7]. Oral administration of RG7388 (25mg/kg/day) to tumor-bearing (KCNR or KP-N-YN cells) mice (once daily for 3 weeks), RG7388 significantly inhibits tumor growth as a monotherapy. In combination with the BCL-2 inhibitor Venetoclax (100mg/kg), RG7388 induces complete remission or partial tumor regression and significantly delays tumor recurrence^[8].

References:

- [1] Higgins B, Glenn K, Walz A, et al. Preclinical optimization of MDM2 antagonist scheduling for cancer treatment by using a model-based approach. Clin Cancer Res. 2014 Jul 15;20(14):3742-52.
- [2] 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.
- [3] Corbali MO, Eskazan AE. Idasanutlin as a new treatment option in improving the therapeutic odyssey of relapsed/refractory AML. Future Oncol. 2020 May;16(14):887-889.
- [4] Mascarenhas J, Lu M, Kosiorek H, et al. Oral idasanutlin in patients with polycythemia vera. Blood. 2019 Aug 8;134(6):525-533.
- [5] Johansson KB, Zimmerman MS, Dmytrenko IV, et al. Idasanutlin and navitoclax induce synergistic apoptotic cell death in T-cell acute lymphoblastic leukemia. Leukemia. 2023 Dec;37(12):2356-2366.
- [6] Isermann T, Schneider KL, Wegwitz F, et al. Enhancement of colorectal cancer therapy through interruption of the HSF1-HSP90 axis by p53 activation or cell cycle inhibition. Cell Death Differ. 2025 Sep;32(9):1734-1749.
- [7] Tucker ER, Jiménez I, Chen L, et al. Combination Therapies Targeting ALK-aberrant Neuroblastoma in Preclinical Models. Clin Cancer Res. 2023 Apr 3;29(7):1317-1331.
- [8] Vernooij L, Bate-Eya LT, Alles LK, et al. High-Throughput Screening Identifies Idasanutlin as a Resensitizing Drug for Venetoclax-Resistant Neuroblastoma Cells. Mol Cancer Ther. 2021 Jun;20(6):1161-1172.

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