

Product Data Sheet

Product Name: Entrectinib

Cat. No.: GC14476

Chemical Properties

Cas. No. 1108743-60-7

Chemical Name (Z)-N-(5-(3,5-difluorobenzyl)-1H-indazol-3(2H)-ylidene)-4-(4-methylpiperazin-1-yl)-2-((tetrahydro-2H-pyran-4-yl)amino)benzamide

SMILES CN1CCN(C2=CC(NC3CCOCC3)=C(C(/N=C4C5=C(NN/4)C=CC(C6=CC(F)=CC(F)=C6)=C5)=O)C=C2)CC1

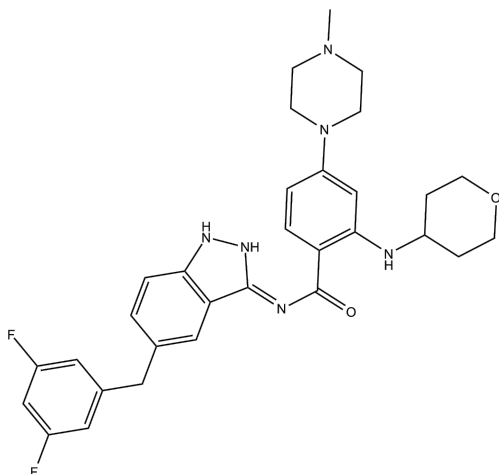
Formula $C_{31}H_{34}F_2N_6O_2$ M.Wt 560.64

Solubility $\geq 28.05\text{mg/mL}$ 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.

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 PC12, HT22 and SK-N-SH cells

The rat adrenal pheochromocytoma cells PC12(FH0415) cells were cultured in RPMI-1640 medium supplemented with 10% fetal bovine serum and 1% penicillin and streptomycin. mouse hippocampal neuron cells HT22 (FH1027) and human neuroblastoma cells SK-N-SH (FH0164) were cultured in DMEM medium with 10% FBS and 1% penicillin and streptomycin. All cells were incubated in a 37°C with 5% CO₂ atmosphere. To explore whether Entrectinib

Preparation Method influences the cellular proliferation ability and apoptosis, cells were treated with 2.3, 4.2 and 4.3μM Entrectinib for 48h, respectively. After incubation, 10μL CCK-8 solution was added into each well and incubated at 37°C for 2h in the dark. Then, a microplate reader was used to measure the absorbance at a wavelength of 450nm. EdU cell proliferation detection kit was used for cell proliferation detection. Annexin V-FITC/PI kit was used for cell apoptosis analysis.

Reaction Conditions 2.3-4.3μM; 48h

Applications Entrectinib dose-dependently reduced viability, suppressed EdU incorporation, and elevated apoptosis in PC12, HT22 and SK-N-SH nerve cells.

Animal experiment [2]:

Animal models athymic nu/nu mice

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Preparation Method	Six-week-old athymic nu/nu mice were obtained from Jackson Laboratories. Mice were maintained at five per cage under humidity- and temperature-controlled conditions in a light/ dark cycle that was set at 12h intervals. For the xenograft studies, animals were injected subcutaneously in the flank with 1×10^7 SY5Y-TrkB cells in 0.1ml of Matrigel. Tumors were measured 2 times per week in 3 dimensions, and the volume calculated as follows: $[(0.523 \times L \times W \times W)/1000]$. Body weights were measured at least twice a week, and the dose of compound was adjusted accordingly. Treatment with Entrectinib, Irino and TMZ started about 15–17 days after tumor inoculation when the average tumor size was 0.2cm^3. Entrectinib was dosed at 60mg/kg BID by gavage for the entire duration of the study(7 weeks). After the final dose was given, the blood samples were drawn from 4 mice per time point via retro-orbital bleeding and collected in heparinized tubes on wet ice. The plasma was then separated by centrifugation at 1200g for 10 minutes at 4°C. The pharmacokinetic analysis was performed using the Watson system. Mice were sacrificed when tumor volume reached 3cm^3. Tumors were harvested and flash frozen on dry ice for analysis of protein expression using Western blot.
Dosage form	60mg/kg; BID for 7 weeks; p.o.
Applications	Entrectinib markedly suppressed SY5Y-TrkB xenograft growth, prolonged mouse event-free survival, and blocked TrkB, Akt and Erk phosphorylation in athymic nu/nu mice.

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References:

- [1] Tang Q, Dong J, Zhang F, et al. Entrectinib can induce nerve cell damage by inhibiting PI3K-AKT and TGF- β signaling pathways. *Front Pharmacol.* 2025;16:1489210.
- [2] Iyer R, Wehrmann L, Golden RL, et al. Entrectinib is a potent inhibitor of Trk-driven neuroblastomas in a xenograft mouse model. *Cancer Lett.* 2016;372(2):179-186.

Background

Entrectinib is an orally active, blood brain barrier(BBB)-penetrated and centrally active inhibitor of TrkA/B/C, ROS1 and ALK, with IC₅₀ values of 1, 3, 5, 12 and 7nM, respectively [1]. TrkA/B/C are neurotrophin receptors, ROS1 is an orphan receptor tyrosine kinase, and ALK is an anaplastic lymphoma kinase; all three drive tumorigenesis through fusion or mutation[2]. Entrectinib is commonly used in the study of ROS1-rearranged non-small cell lung cancer (NSCLC) and NTRK fusion-positive solid tumors[3].

In vitro, Entrectinib (2.3-4.3 μ M; 48h) dose-dependently reduced viability, suppressed colony formation and EdU incorporation, and elevated apoptosis in PC12, HT22 and SK-N-SH nerve cells, with cellular IC₅₀ values of 2.3, 4.2 and 4.3 μ M, respectively [4]. Entrectinib (100-400nM; 24h) dose-dependently inhibited TGF- β 1-driven proliferation, migration, and myofibroblast activation of Mlg and HFL1 lung fibroblasts and blocked TGF- β 1-induced epithelial-mesenchymal transition (EMT) in MLE12 epithelial cells[5].

In vivo, Entrectinib (60mg/kg; BID for 7 weeks; p.o.) markedly suppressed SY5Y-TrkB xenograft growth, prolonged mouse event-free survival, and blocked TrkB, Akt and Erk phosphorylation in athymic nu/nu mice[6]. Entrectinib (10mg/kg; i.p.) reduced LPS-induced serum IL-1 β and hepatic AST/ALT levels, and improved 24h survival in C57BL/6J mice[7].

References:

- [1] Ardini E, Menichincheri M, Banfi P, et al. Entrectinib, a Pan-TRK, ROS1, and ALK Inhibitor with Activity in Multiple Molecularly Defined Cancer Indications. *Mol Cancer Ther.* 2016;15(4):628-639.
- [2] Drilon A, Siena S, Ou SI, et al. Safety and Antitumor Activity of the Multitargeted Pan-TRK, ROS1, and ALK Inhibitor Entrectinib: Combined Results from Two Phase I Trials (ALKA-372-001 and

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STARTRK-1). *Cancer Discov.* 2017;7(4):400-409.

[3] Osman HM, Tuncbilek M. Entrectinib: A New Selective Tyrosine Kinase Inhibitor Approved for the Treatment of Pediatric and Adult Patients with NTRK Fusionpositive, Recurrent or Advanced Solid Tumors. *Curr Med Chem.* 2022;29(15):2602-2616.

[4] Tang Q, Dong J, Zhang F, et al. Entrectinib can induce nerve cell damage by inhibiting PI3K-AKT and TGF- β signaling pathways. *Front Pharmacol.* 2025;16:1489210.

[5] Miao Y, Li X, Yang Y, et al. Entrectinib ameliorates bleomycin-induced pulmonary fibrosis in mice by inhibiting TGF- β 1 signaling pathway. *Int Immunopharmacol.* 2022;113(Pt B):109427.

[6] Iyer R, Wehrmann L, Golden RL, et al. Entrectinib is a potent inhibitor of Trk-driven neuroblastomas in a xenograft mouse model. *Cancer Lett.* 2016;372(2):179-186.

[7] Jin X, Liu D, Zhou X, Luo X, Huang Q, Huang Y. Entrectinib inhibits NLRP3 inflammasome and inflammatory diseases by directly targeting NEK7. *Cell Rep Med.* 2023;4(12):101310.

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