Entrectinib

Cat. No.: HY-12678

CAS No.: 1108743-60-7

Molecular Formula: $C_{31}H_{34}F_2N_6O_2$

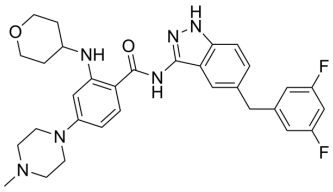
Molecular Weight: 560.64

Target: ROS Kinase; Trk Receptor; Anaplastic lymphoma kinase (ALK); Autophagy

Pathway: Protein Tyrosine Kinase/RTK; Neuronal Signaling; Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 31 mg/mL (55.29 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7837 mL	8.9184 mL	17.8368 mL
	5 mM	0.3567 mL	1.7837 mL	3.5674 mL
	10 mM	0.1784 mL	0.8918 mL	1.7837 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 0.5% MC >> 0.5% Tween-80
   Solubility: 5 mg/mL (8.92 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.5 mg/mL (4.46 mM); Clear solution
3. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.46 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (3.71 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (3.71 mM); Suspended solution; Need ultrasonic
6. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.71 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Entrectinib (NMS-E628) is a potent, orally available, and CNS-active pan-Trk, ROS1, and ALK inhibitor. Entrectinib inhibits TrkA, TrkB, TrkC, ROS1 and ALK with IC_{50} values of 1, 3, 5, 12 and 7 nM, respectively. Antitumor activity.		
IC_{50} & Target	TrkA	TrkB	TrkC
In Vitro	Entrectinib (NMS-E628) is found to be exquisitely active in inhibiting the proliferation of a limited number of cell lines: the TRKA-driven colorectal carcinoma cell line KM12 (IC_{50} of 17 nM), the ALK-dependent ALCL cell lines SU-DHL-1, Karpas-299, SUP-M2 and SR-786 (IC_{50} of 20, 31, 41, and 81 nM, respectively), the ALK-dependent NSCLC cell line NCI-H2228 (IC_{50} of 68 nM) and the FLT3-dependent AML cell line MV-4-11 (IC_{50} of 81 nM). Entrectinib potently blocks proliferation of Ba/F3-TEL-TRKB (IC_{50} of 2.9 nM), Ba/F3-TEL-TRKC (IC_{50} of 3.3 nM), and Ba/F3-TEL-ROS1 (IC_{50} of 5.3 nM) cells, with a high degree of selectivity versus parental Ba/F3 cells or those transformed by nontargeted kinases such as ABL and RET, which are inhibited with IC_{50}s in the range of 2 to 3 μM[1]. Entrectinib significantly inhibits the growth of TrkB-expressing NB cells in vitro, and it significantly enhances the growth inhibition of Irino-TMZ when used in combination[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		
In Vivo	Oral administration of entrectinib to tumor-bearing mice induces regression in relevant human xenograft tumors, including the TRKA-dependent colorectal carcinoma KM12, ROS1-driven tumors, and several ALK-dependent models of different tissue origins, including a model of brain-localized lung cancer metastasis[1]. Single agent therapy results in significant tumor growth inhibition in animals treated with entrectinib compared to control animals[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		

PROTOCOL

Cell Assay [2]	NLF, NLF-TrkB, SY5Y or SY5Y-TrkB cells are plated in 96 well plates, and they are exposed to drug at different concentrations (1, 5, 10, 20, 30, 50 and 100 nM of entrectinib, 1.5 μM Irino and 50 μM TMZ, respectively) for one hr followed by addition of 100 ng/mL of BDNF. Plates are harvested at 24, 48, and 72 hr following addition of drug. The plates are processed and cell viability is analyzed using a standard SRB assay protocol[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice: Entrectinib is reconstituted in 0.5% methylcellulose containing 1% Tween 80 at a final dosing volume of 10 mL/kg (e.g., 0.2 mL for a 20 gm mouse). Treatment with entrectinib, Irino and TMZ started about 15–17 days after tumor inoculation when the average tumor size is 0.2 cm^3. Mice are sacrificed when tumor volume reached 3 cm^3. Tumors are harvested and flash frozen on dry ice for analysis of protein expression[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nature. 2021 Jun;594(7862):277-282.
- Science. 2017 Dec 1;358(6367):eaan4368.
- Nat Commun. 2021 Feb 24;12(1):1261.
- Cell Rep Med. 2023 Jan 10;100911.
- Cell Rep. 2020 Aug 4;32(5):107994.

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REFERENCES

[1]. Ardini E, et al. Entrectinib, a Pan-TRK, ROS1, and ALK Inhibitor with Activity in Multiple Molecularly Defined Cancer Indications. Mol Cancer Ther. 2016 Apr;15(4):628-39.

[2]. Iyer R, et al. Entrectinib is a potent inhibitor of Trk-driven neuroblastomas in a xenograft mouse model. Cancer Lett. 2016 Mar 28;372(2):179-86.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA