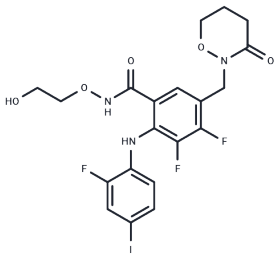
Data Sheet (Cat.No.T5412)

TargetMol

RO4987655

Chemical Properties



CAS No. : 874101-00-5

Formula: C20H19F3IN3O5

Molecular Weight: 565.28

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	RO4987655 (RG7167) is an orally active and highly selective MEK inhibitor (IC50: 5.2 nM for MEK1/MEK2).
Targets(IC50)	MEK
In vitro	CH4987655 (RO4987655) potently inhibits mitogen-activated protein kinase signaling pathway activation and tumor cell growth, with an in vitro IC50 of 5.2 nmol/L for inhibition of MEK1/2 [1]. In NCI-H2122 cells, RO4987655 at doses ranging from 0.1 to 1.0 μM suppressed pERK1/2 already at 2 h after the start of treatment. RO4987655 inhibited proliferation of NCI-H2122 cells in a dose-dependent manner with an IC50 value of 0.0065 μM [2].
In vivo	In the dose-ranging study, treatment with RO4987655 5.0 mg/kg led to dramatic decrease in FDG uptake on day 1. The daily RO4987655, 2.5 mg/kg treatment were followed by PET examinations on days 1, 3, and 9 of the drug administration. The maximum decrease was observed on day 1, followed by a slight rebound on day 3. The effect plateaued thereafter to day 9 of treatment [2]. Doses of 0.5, 1, 2, 3, and 4 mg were safe and well-tolerated. A total of 26 adverse events (n = 15) were reported: 21 mild, 5 moderate, and none severe. Moderate adverse events were experienced by one subject at 1 mg (autonomic nervous system imbalance) and three subjects at 4 mg (diarrhea, abdominal pain, autonomic nervous system, and acne) [3].
Cell Research	Cells were treated with various concentrations of RO4987655 for 72 h in 96-well plates and viable cells were quantified with Cell Counting Kit-8. For Western blotting, cells were treated with RO4987655 for indicated periods and lysed with cell lysis buffer containing a protease inhibitor cocktail, phosphatase inhibitor cocktails 2 and 3, and 1 mM PMSF. For detection of protein bands, the following were used as primary antibodies: pEGFR, EGFR, pMKK4, MKK4, pAKT, AKT, pERK, ERK, pMEK1/2, MEK, Cyclin D1, and actin. All protein bands were visualized with secondary antibodies labeled with HRP and ECL system by using ImageQuant LAS 4000 [2].
Animal Research	A time interval of 20 to 24 h was used between daily RO4987655 administration and completion of PET imaging for each tumor-bearing mouse and for each PET imaging time point (day 0, 1, 3 and 9). Mice were fasted for 6 to 8 h prior to start of the imaging session. [18F] FDG (7 to 8 MBq per mouse, maximum volume of 200 μL) was administered to awake, warmed (37°C) mice by a bolus injection via the tail vein. Forty to sixty minutes after the tracer injection, the mice were administered with isoflurane,

Animal Research	controlled by an E-Z anesthesia vaporizer. The mice were placed on a heated pad (37°C) on the camera bed, with most of the body volume in the field of view (7.68 cm). Emission data were collected for 20 min in list mode with a microPET Focus 120 scanner. Maximum standardized uptake values (SUVmax) of [18F] FDG uptake in the tumor were calculated and normalized to the administered activity (MBq/body weight, g). The drug effect on tumor metabolism was estimated as%SUVmax change to day 0 (baseline) [2].

Solubility Information

Solubility	DMSO: 35 mg/mL (61.92 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (3.54 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.769 mL	8.8452 mL	17.6903 mL
5 mM	0.3538 mL	1.769 mL	3.5381 mL
10 mM	0.1769 mL	0.8845 mL	1.769 mL
50 mM	0.0354 mL	0.1769 mL	0.3538 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Lee L, et al. The safety, tolerability, pharmacokinetics, and pharmacodynamics of single oral doses of CH4987655 in healthy volunteers: target suppression using a biomarker. Clin Cancer Res. 2009 Dec 1;15(23):7368-74.
Tegnebratt T, et al. Evaluation of efficacy of a new MEK inhibitor, RO4987655, in human tumor xenografts by [(18)F] FDG-PET imaging combined with proteomic approaches. EJNMMI Res. 2014 Dec;4(1):34.