Zeteletinib

Cat. No.: HY-139590

CAS No.: 2216753-97-6

Molecular Formula: $C_{25}H_{23}F_3N_4O_4$

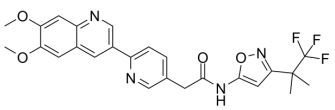
Molecular Weight: 500.47

Target: RET; PDGFR

Pathway: Protein Tyrosine Kinase/RTK

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 : 100 mg/mL (199.81 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9981 mL	9.9906 mL	19.9812 mL
5 mM	0.3996 mL	1.9981 mL	3.9962 mL
10 mM	0.1998 mL	0.9991 mL	1.9981 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.00 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.00 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.00 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Zeteletinib (BOS-172738; DS-5010) is an orally active, selective RET kinase inhibitor with nanomolar potency against RET and >300-fold selectivity against VEGFR2. Zeteletinib shows exquisite potency for the wild type RET, $RET^{V804M/L}$ gatekeeper mutants, and the most common oncogenic RET mutation M918T. Zeteletinib has potent antitumor activity[1][2][3].

IC_{50} & Target

PDGFR2

In Vitro

In biochemical assays of 106 kinases, RET and platelet-derived growth factor receptor (PDGFR) alpha/beta were inhibited

	more than 80% by 193 nM Zeteletinib (BOS-172738; DS-5010). The IC_{50} values of Zeteletinib against RET, RET-GKm (V804L) were single digit nano-molar even under a condition of high concentration of ATP; besides it against KDR was more than 1000 nM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	In a Ba/F3-RET subcutaneous tumor model, Zeteletinib (BOS-172738; DS-5010) dosing at 10 mg/kg twice daily (bid) induces tumor regression[1]. In an LC2/ad NSCLC xenograft model, which has the RET-CCDC6 fusion gene, Zeteletinib dosing at 1 mg/kg thrice daily (tid) induced tumor regression[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Yasuyuki Kaneta, et al.Abstract B173: Preclinical characterization and antitumor efficacy of DS-5010, a highly potent and selective RET inhibitor. MOLECULAR CANCERTHERAPEUTICS. January 2018, Volume 17, Issue 1.

[2]. Patrick Schoffski, et al. BOS172738, a highly potent and selective RET inhibitor, for the treatment of RET-altered tumors including RET-fusion+ NSCLC and RET-mutant MTC: Phase 1 study results. Journal of Clinical Oncology 39, no. 15_suppl (May 20, 2021) 3008-3008.

[3]. Kyaw Z Thein, et al. Precision therapy for RET-altered cancers with RET inhibitors. Trends Cancer. 2021 Dec;7(12):1074-1088.

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