Pamufetinib mesylate

Cat. No.: HY-12423A

CAS No.: 1688673-09-7

Molecular Formula: $C_{28}H_{27}FN_4O_7S_2$

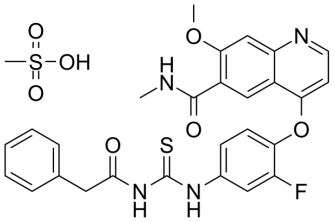
Molecular Weight: 614.66

Target: VEGFR; c-Met/HGFR

Pathway: Protein Tyrosine Kinase/RTK

Storage: 4°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 75 mg/mL (122.02 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.6269 mL	8.1346 mL	16.2692 mL
5 mM	0.3254 mL	1.6269 mL	3.2538 mL
10 mM	0.1627 mL	0.8135 mL	1.6269 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.07 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.07 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Pamufetinib (TAS-115) mesylate is a potent VEGFRand hepatocyte growth factor receptor (c-Met/HGFR)-targeted kinase inhibitor, with IC_{50}s of 30 and 32 nM for rVEGFR2 and rMET, respectively.

IC_{50} & Target

IC50: 30 nM (rVEGFR2), 32 nM (rMET)[1]

In Vitro

Pamufetinib mesylate powerfully suppresses the VEGF-dependent proliferation of HUVECs (IC_{50}=0.019 μM) as a VEGFR-targeted inhibitor and powerfully suppresses the proliferation of MET-amplified cancer cells (GI_{50}=0.032-0.362 μM) as a MET-targeted inhibitor. Pamufetinib mesylate has much less toxicity in various normal cell lines when compared with other VEGFR-targeted kinase inhibitors[1]. Crizotinib and Pamufetinib mesylate inhibit Met phosphorylation and reverse erlotinib resistance and VEGF production triggered by HGF in PC-9 and HCC827 cells[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo	Pamufetinib mesylate completely suppresses the progression of MET-inactivated tumor by blocking angiogenesis without toxicity when given every day for 6 weeks, even at a serum-saturating dose of Pamufetinib mesylate. Pamufetinib mesylate induces marked tumor shrinkage and prolongs survival in MET-amplified human cancer–bearing mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Tumor cells (8000 cells/800 mL) with or without TAS-115 (1.0 μM) or erlotinib (0.3 μM) in the lower Transwell collagen–coated chambers are cocultured with MRC-5 (1000 cells/300 μL) cells in the upper chamber for 72 hours. The upper chamber is then removed. Cell viability is measured using the MTT assay[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] The TAS-115 dose levels are set at 12.5, 50, and 200 mg/kg/d. The dose level for sunitinib is set at 40 mg/kg/d. Oral drug treatment is continued for 14 or 42 consecutive days for the chronic dosing in the SC-9 xenograft model. During the treatment period, TV and body weight are measured twice per week. The antitumor efficacy is assessed at the end of each study period[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Fujita H, et al. The novel VEGF receptor/MET-targeted kinase inhibitor TAS-115 has marked in vivo antitumor properties and a favorable tolerability profile. Mol Cancer Ther. 2013 Dec;12(12):2685-96.

[2]. Nakade J, et al. Triple inhibition of EGFR, Met, and VEGF suppresses regrowth of HGF-triggered, erlotinib-resistant lung cancer harboring an EGFR mutation. J Thorac Oncol. 2014 Jun;9(6):775-83.

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