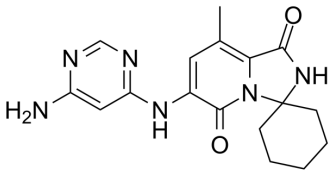
Tomivosertib

Cat. No.:	HY-100022
CAS No.:	1849590-01-7
Molecular Formula:	$C_{17}H_{20}N_6O_2$
Molecular Weight:	340.38
Target:	MNK; PD-1/PD-L1
Pathway:	MAPK/ERK Pathway; Immunology/Inflammation
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 : 4.35 mg/mL (12.78 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.9379 mL	14.6895 mL	29.3789 mL
	5 mM	0.5876 mL	2.9379 mL	5.8758 mL
	10 mM	0.2938 mL	1.4689 mL	2.9379 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.44 mg/mL (1.29 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 0.43 mg/mL (1.26 mM); Clear solution
3. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: 0.4 mg/mL (1.18 mM); Suspended solution; Need ultrasonic
4. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: 0.4 mg/mL (1.18 mM); Suspended solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

Tomivosertib (eFT508) is a potent, highly selective, and orally active MNK1 and MNK2 inhibitor, with IC_{50}s of 1-2 nM against both isoforms. Tomivosertib (eFT508) treatment leads to a dose-dependent reduction in eIF4E phosphorylation at serine 209 (IC_{50}=2-16 nM) in tumor cell lines[1]. Tomivosertib (eFT508) also dramatically downregulates PD-L1 protein abundance[2].

IC_{50} & Target	MNK1 1-2 nM (IC_{50})	MNK2 1-2 nM (IC_{50})	PD-L1
In Vitro	Tomivosertib (eFT508) reduces eIF4E phosphorylation dose-dependently at serine 209 (IC_{50}=2-16 nM) in tumor cell lines. In a panel of appr 50 hematological cancers, Tomivosertib shows anti-proliferative activity against multiple DLBCL cell lines. Sensitivity to Tomivosertib in TMD8, OCI-Ly3 and HBL1 DLBCL cell lines is associated with dose-dependent decreases in production of pro-inflammatory cytokines including TNFα, IL-6, IL-10 and CXCL10. Further evaluation Tomivosertib mechanism of action demonstrates that decreased TNFα production correlates with a 2-fold decrease in TNFα mRNA half-life[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		
In Vivo	Tomivosertib (eFT508) shows significant anti-tumor activity in the TMD8 and HBL-1 ABC-DLBCL models, both of which harbor activating MyD88 mutations. Besides, Tomivosertib combines effectively with components of R-CHOP and with novel targeted agents, including PCI-32765 and Venetoclax, in human lymphoma models[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.		

CUSTOMER VALIDATION

- Nat Chem Biol. 2022 Jun 13.
- Oncogene. 2021 Feb 9.
- PLoS Biol. 2022 Jun 1;20(6):e3001653.
- Front Endocrinol. 2023 May 25;14:1139874.

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REFERENCES

[1]. Kevin R. Webster, et al. eFT508, a Potent and Selective Mitogen-Activated Protein Kinase Interacting Kinase (MNK) 1 and 2 Inhibitor, Is Efficacious in Preclinical Models of Diffuse Large B-Cell Lymphoma (DLBCL). Blood 2015 126:1554.

[2]. Xu Y, et al. Translation control of the immune checkpoint in cancer and its therapeutic targeting. Nat Med. 2019 Feb;25(2):301-311.

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