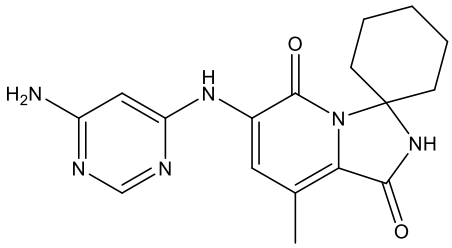
Catalog #10-4081

eFT508

CAS# 1849590-01-7

6-[(6-Aminopyrimidin-4-yl)amino]-8-methylspiro[2H-imidazo[1,5-a]pyridine-3,1'-cyclohexane]-1,5-dione; Tomivosertib

Lot # FBS4026



eFT508 is a potent (IC_{50}s = 2.4 nM MNK1; 1.0 nM MNK2) and highly selective inhibitor of the mitogen-activated protein kinase interacting kinases 1 and 2 (MNK1/2), key regulators of mRNA translation protein eukaryotic initiation factor eIF4E.[1] It potently inhibits phosphorylation of eIF4E in multiple solid and hematological tumor lines leading to blockade of pro-inflammatory and pro-tumorigenic cytokine production. eFT508 reversed the aggressive and metastatic characteristics of mouse liver cancer *via* inhibition of PD-L1 upregulation.[2] Displays inhibitory effects in various cancers models including acute myeloid leukemia[3], gastric[4], and breast[5]. eFT-508 has also shown efficacy in treating neuropathic pain *via* the MNK-eIF4E pathway.[6,7,8]

1) Reich *et al.* (2018), *Structure-based design of Pyridone-Aminal eFT508 Targeting Dysregulated Translation by Selective Mitogen-activated Protein Kinase Interacting Kinases 1 and 2 (MNK1/2) Inhibition*; J.Med.Chem. **61** 3516
2) Xu *et al.* (2019), *Translation control of the immune checkpoint in cancer and its therapeutic targeting*; Nat. Med. **25** 301
3) Suarez *et al.* (2021), *Inhibitory effects of Tomivosertib in acute myeloid leukemia*; Oncotarget **12** 955
4) Yang *et al.* (2022), *Inhibition MNL-eIF4E-ß-catenin preferentially sensitizes gastric cancer to chemotherapy*; Fundam. Clin. Pharmacol. **36** 712
5) Yang *et al.* (2022), *Treatment with eFT-508 increases chemosensitivity in breast cancer cells by modulating the tumor microenvironment*; J. Transl. Med. **20** 276
6) Megat *et al.* (2019), *Nociceptor Translational Profiling Reveals the Ragulator-Rag GTPase Complex as a Critical Generator of Neuropathic Pain*; J. Neurosci. **39** 393
7) Shiers *et al.* (2020), *Reversal of peripheral nerve injury-induced neuropathic pain and cognitive dysfunction via genetic and tomivosertib targeting of MNK*; Neuropsychopharmacology **45** 524
8) Jeevakumar *et al.* (2020), *IL-6 induced upregulation of T-type Ca2+ currents and sensitization of DRG nociceptors is attenuated by MNK inhibition*; J. Neurophysiol. **124** 274

PHYSICAL DATA

Molecular Weight:	340.39
Molecular Formula:	$C_{17}H_{20}N_6O_2$
Purity:	98% (HPLC)
	NMR: (Conforms)
Solubility:	DMSO (2 mg/mL with warming)
Physical Description:	Pale yellow solid
Storage and Stability:	Store as supplied at -20°C for up to 2 years from the date of purchase. Solutions in DMSO may be stored at -20°C for up to 3 months.

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