产品名称：eFT508
产品别名：Tomivosertib

生物活性：

Description

Tomivosertib (eFT508) is a potent, highly selective, and orally bioavailable MNK1 and MNK2 inhibitor, with IC50s of 1-2 nM against both isoforms. Treatment of tumor cell lines with Tomivosertib (eFT508) leads to a dose-dependent reduction in eIF4E phosphorylation at serine 209 (IC50=2-16 nM)[1]. Tomivosertib (eFT508) also dramatically downregulates PD-L1 protein abundance[2].

IC_{50} & Target

MNK1	MNK2	PD-L1
1-2 nM (IC_{50})	1-2 nM (IC_{50})	

In Vitro

Tomivosertib (eFT508) reduces eIF4E phosphorylation dose-dependently at serine 209 (IC50=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].

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].

Solvent&Solubility

In Vitro:

DMSO : 4.35 mg/mL (**12.78 mM;** Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / 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

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 0.43 mg/mL (1.26 mM); Clear solution

此方案可获得 ≥ 0.43 mg/mL (1.26 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 4.3 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。

	2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 0.44 mg/mL (1.29 mM); Clear solution 此方案可获得 ≥ 0.44 mg/mL (1.29 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 4.4 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.