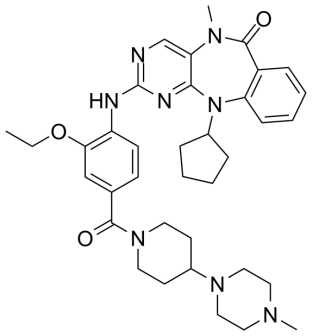
XMD17-109

Cat. No.:	HY-15665
CAS No.:	1435488-37-1
Molecular Formula:	$C_{36}H_{46}N_8O_3$
Molecular Weight:	638.8
Target:	ERK
Pathway:	MAPK/ERK Pathway; Stem Cell/Wnt
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (156.54 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5654 mL	7.8272 mL	15.6544 mL
	5 mM	0.3131 mL	1.5654 mL	3.1309 mL
	10 mM	0.1565 mL	0.7827 mL	1.5654 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 (3.91 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (3.91 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.91 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

XMD17-109 is a novel, specific ERK-5 inhibitor, with an IC_{50} of 162 nM.

IC_{50} & Target

ERK5	LRRK2[G2019S]
162 nM (IC_{50})	339 nM (IC_{50})

In Vitro

XMD17-109 (Compound 26) inhibits ERK5 biochemically with an IC_{50} of 0.162 ± 0.006 μM, and blocks pidermal growth factor induced ERK5 autophosphorylation with an EC_{50} of 0.09 ± 0.03 μM in cells. XMD17-109 also inhibits LRRK2[G2019S] with an

IC_{50} of 339 nM[1]. XMD17-109 demonstrats low nanomolar cellular activity judged by the significant dose-dependent reduction of mobility shifted phosphorylated ERK5 bands from sorbitol stimulated cells. XMD17-109 completely inhibits the ERK5-mediated AP1 transcriptional activity at 30 μM and has an EC_{50} of 4.2 μM[2].

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

PROTOCOL

Cell Assay [2]

HeLa cells are maintained in DMEM supplemented with 10% FBS, 2 mM l-glutamine, 50 U/mL penicillin G, and 50 μg/mL streptomycin. Before use HeLa cells are serum starved for 16 h in DMEM supplemented with 2 mM l-glutamine, 50 U/mL penicillin G, and 50 μg/mL streptomycin. HeLa cells are then incubated with ERK5-IN-1 at the indicated concentrations for 1 h prior to stimulation with 0.5mol/Lsorbitol for 30 min. Cells are lysed in Triton lysis buffer (50 mM Tris-HCl, pH 7.5, 1 mM EGTA, 1 mM EDTA, 1 mM sodium orthovanadate, 50 mM sodium fluoride, 1 mM sodium pyrophosphate, 0.27mol/Lsucrose, 1 μM microcystin-LR, 1% (v/v) Triton X-100, 0.1% (v/v) 2-mercaptoethanol) and 20 μg of protein loaded per well. Samples are run on 8% polyacrylamide gels using standard methods. Proteins are transferred onto nitrocellulose membranes and specific proteins detected by immunoblotting.

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

CUSTOMER VALIDATION

- Cancer Lett. 2021 Jul 7;S0304-3835(21)00334-7.
- Sci Signal. 2015 Aug 25;8(391):ra86.
- Patent. US20220378919A1.
- Ann Transl Med. 2019 Oct;7(20):561.
- Oncotarget. 2016 Jun 7;7(23):34322-40.

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REFERENCES

[1]. Deng X, et al. Structural determinants for ERK5 (MAPK7) and leucine rich repeat kinase 2 activities of benzo[e]pyrimido-[5,4-b]diazepine-6(11H)-ones. Eur J Med Chem. 2013;70:758-67.

[2]. Elkins, Jonathan M., et al. X-ray Crystal Structure of ERK5 (MAPK7) in Complex with a Specific Inhibitor. Journal of Medicinal Chemistry (2013), 56(11), 4413-4421.

[3]. Wilhelmsen K, et al. Extracellular signal-regulated kinase 5 promotes acute cellular and systemic inflammation. Sci Signal. 2015 Aug 25;8(391):ra86.

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