Web: www.taiclone.com
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XMD8-92

Catalog No: tcsc0245

Available Sizes

Size: 10mg

Size: 50mg

Size: 100mg

Specifications

CAS No:
1234480-50-2

Formula:
$C_{26}H_{30}N_6O_3$

Pathway:
Stem Cell/Wnt;MAPK/ERK Pathway

Target:
ERK;ERK

Purity / Grade:
>98%

Solubility:
DMSO : 50 mg/mL (105.36 mM; Need ultrasonic)

Observed Molecular Weight:
474.55

Product Description

XMD8-92 is a highly selective **ERK5/BMK1** inhibitor with dissociation constant ($\mathbf{K_d}$) value of 80 nM.

IC50 & Target: Kd: 80 nM (ERK5/BMK1)[1]

In Vitro:

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XMD8-92 exhibits the greatest affinity towards BMK1 with a measured dissociation constant (K_d) of 80 nM, while DCAMKL2, TNK1 and PLK4 exhibit K_d's of 190, 890 and 600 nM, respectively. XMD8-92 is profiled against all detectable kinases in HeLa cell lysates using the KiNativ method and is found to be about 10-fold more selective for BMK1 with a IC_{50} of 1.5 μM than the most potent off-targets, TNK1 (IC_{50}=10 μM) and ACK1 (aka TNK2, IC_{50}=18 μM). Other weak off-targets include the kinase domain 2 of RSK1 and RSK2, PIK4A and PIK4B, and FAK. Notably, MEK5 is not significantly inhibited by XMD8-92 at up to 50 μM[1]. XMD8-92 shows high selectivity to BMK1 in an in vitro ATP-site competition binding assay against 402 kinases as well as in the KiNativ method against all detectable kinases in HeLa cell lysates. XMD8-92 blocks EGF-induced activation of BMK1 with IC_{50} of 240 nM and, with concentration as high as 5 μM, XMD8-92 has no inhibitory effect on ERK1/2 activation by EGF[2].

In Vivo: XMD8-92 significantly inhibits tumor growth in vivo by 95%. The pharmacokinetics of XMD8-92 is evaluated in Sprague-Dawley rats given a single intravenous or oral dose. XMD8-92 is found to have a 2.0 hr half life clearance of 26 mL/min/kg. XMD8-92 has moderate tissue distribution with a calculated volume of distribution of 3.4 L/kg. XMD8-92 has high oral bioavailability with 69% of the dose absorbed. After a single oral dose of 2 mg/kg, maximal plasma concentrations of approximately 500 nM are observed by 30 minutes, with 34 nM remaining 8 hr post dose. In tolerability experiments, high plasma concentrations of drug (approximately 10 μM following IP dosing of 50 mg/kg) are maintained throughout the 14 days. XMD8-92 appears to be well tolerated and the mice appeared healthy with no sign of distress. No vasculature instability is observed in the XMD8-92-treated mice[1]. XMD8-92 treatment in both immunocompetent and immunodeficient mice blocked the growth of lung and cervical xenograft tumors, respectively, by 95%. This remarkable anti-tumor effect of XMD8-92 in lung and cervical xenograft tumor models is due to XMD8-92's capacity to inhibit tumor cell proliferation through the PML suppression-inducted p21 checkpoint protein, and by blocking of BMK1's contribution in tumor-associated angiogenesis. Besides, BMK1 knockout (KO) in mice leads to complete and irreversible removal of the BMK1 protein, while XMD8-92 treatment in mice only suppresses the activity of BMK1, which is reversible. Second, the vasculature instability observed in BMK1 KO mice may be due to lack of the C-terminal non-kinase domain of BMK1, which is still present during XMD8-92 treatment of animals[2].