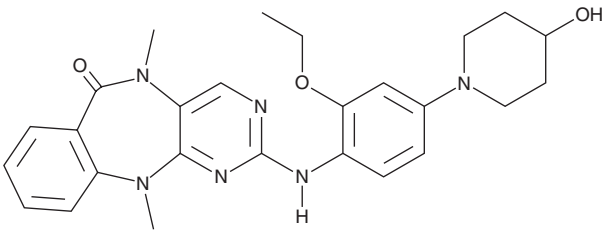
PRODUCT INFORMATION

XMD8-92

Item No. 19173

CAS Registry No.:	1234480-50-2
Formal Name:	2-[[2-ethoxy-4-(4-hydroxy-1-piperidinyl)phenyl]amino]-5,11-dihydro-5,11-dimethyl-6H-pyrimido[4,5-b][1,4]benzodiazepin-6-one
MF:	$C_{26}H_{30}N_6O_3$
FW:	474.6
Purity:	≥95%
UV/Vis.:	λ_{max}: 210, 293 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

XMD8-92 is supplied as a crystalline solid. A stock solution may be made by dissolving the XMD8-92 in the solvent of choice. XMD8-92 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, which should be purged with an inert gas. The solubility of XMD8-92 in these solvents is approximately 1 mg/ml.

Description

XMD8-92 is an ERK5 inhibitor (K_d = 80 nM) that less potently inhibits DCAMKL2, TNK1, and Plk4 (K_ds = 190, 890, and 600 nM, respectively) in a panel of 402 kinases.[1] It blocks ERK5 autophosphorylation, ERK5-mediated phosphorylation of promyelocytic leukemia protein (PML), and PML-dependent activation of p21.[1] XMD8-92 inhibits AP-1 transcriptional activity induced by MEK5-activated ERK5 but not that induced by Cdc37.[2] It inhibits bFGF-induced angiogenesis in a Matrigel™ plug assay in mice and reduces tumor growth in a HeLa mouse xenograft model when administered at a dose of 50 mg/kg twice per day.[1] XMD8-92 also binds bromodomain-containing protein 4 (BRD4; K_d = 170 nM for BRD4 bromodomain 1).[3]

References

1. Yang, Q., Deng, X., Lu, B., *et al.* Pharmacological inhibition of BMK1 suppresses tumor growth through promyelocytic leukemia protein. *Cancer Cell* **18(3)**, 258-267 (2010).
2. Erazo, T., Moreno, A., Ruiz-Babot, G., *et al.* Canonical and kinase activity-independent mechanisms for extracellular signal-regulated kinase 5 (ERK5) nuclear translocation require dissociation of Hsp90 from the ERK5-Cdc37 complex. *Mol. Cell Biol.* **33(8)**, 1671-1686 (2013).
3. Lin, E.C.K., Amantea, C.M., Nomanbhoy, T.K., *et al.* ERK5 kinase activity is dispensable for cellular immune response and proliferation. *Proc. Natl. Acad. Sci. U.S.A.* **113(42)**, 11865-11870 (2016).

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