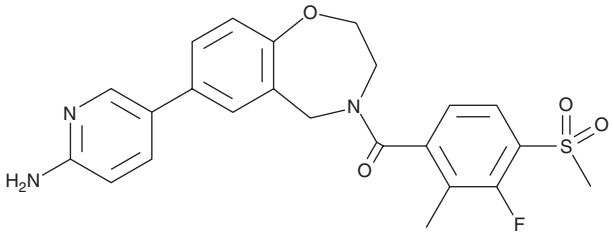
PRODUCT INFORMATION

XL388

Item No. 20237

CAS Registry No.:	1251156-08-7
Formal Name:	[7-(6-amino-3-pyridinyl)-2,3-dihydro-1,4-benzoxazepin-4(5H)-yl][3-fluoro-2-methyl-4-(methylsulfonyl)phenyl]-methanone
MF:	$C_{23}H_{22}FN_3O_4S$
FW:	455.5
Purity:	≥98%
UV/Vis.:	λ_{max}: 275 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

XL388 is supplied as a crystalline solid. A stock solution may be made by dissolving the XL388 in the solvent of choice. XL388 is soluble in the organic solvent DMSO (warmed), at a concentration of approximately 5 mg/ml.

Description

XL388 is an orally bioavailable and ATP-competitive inhibitor of mammalian target of rapamycin (mTOR; IC_{50} = 9.9 nM).[1] It is selective for mTOR over a panel of more than 140 kinases, including various PI3Ks (IC_{50}s = >3,000 nM). It inhibits mTOR complex 1 (mTORC1) and mTORC2 *in vitro* (IC_{50}s = 8 and 166 nM, respectively).[2] XL388 induces cytotoxicity in MG-63, U2OS, and Saos-2 osteosarcoma and 786-0 kidney cancer cells and increases apoptosis in 786-0 and MG-63 cells in a concentration-dependent manner.[3,4] It also induces cell cycle arrest at the G_1 phase and increases autophagy in MG-63 cells.[3] XL388 (50 and 100 mg/kg) reduces tumor growth in an MCF-7 breast cancer mouse xenograft model and inhibits phosphorylation of the mTORC1 and mTORC2 substrates p70S6K, S6, 4E-BP1, and Akt in MCF-7 and PC-3 xenograft tumors when administered at a dose of 100 mg/kg.[1] XL388 (20 mg/kg) also reduces tumor growth in U2OS and 786-0 mouse xenograft models.[3,4]

References

1. Takeuchi, C.S., Kim, B.G., Blazey, C.M., *et al.* Discovery of a novel class of highly potent, selective, ATP-competitive, and orally bioavailable inhibitors of the mammalian target of rapamycin (mTOR). *J. Med. Chem.* **56(6)**, 2218-2234 (2013).
2. Miller, N. Abstract B146: XL388: A novel, selective, orally bioavailable mTORC1 and mTORC2 inhibitor that demonstrates pharmacodynamic and antitumor activity in multiple human cancer xenograft models. *Mol. Cancer Ther.* **8(Suppl 12)**, B146 (2009).
3. Zhu, Y.-R., Zhou, X.-Z., Zhu, L.-Q., *et al.* The anti-cancer activity of the mTORC1/2 dual inhibitor XL388 in preclinical osteosarcoma models. *Oncotarget* **7(31)**, 49527-49538 (2016).
4. Xiong, Z., Zang, Y., Zhong, S., *et al.* The preclinical assessment of XL388, a mTOR kinase inhibitor, as a promising anti-renal cell carcinoma agent. *Oncotarget* **8(18)**, 30151-30161 (2017).

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