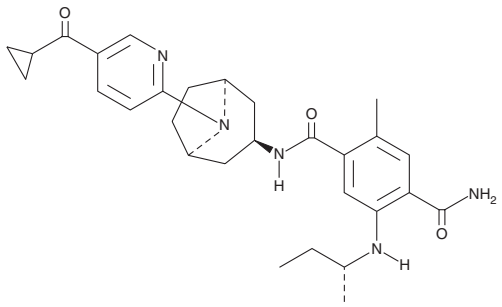
PRODUCT INFORMATION

XL888

Item No. 16309

CAS Registry No.:	1149705-71-4
Formal Name:	N^1-[(3-endo)-8-[5-(cyclopropylcarbonyl)-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]-2-methyl-5-[[(1R)-1-methylpropyl]amino]-1,4-benzenedicarboxamide
MF:	$C_{29}H_{37}N_5O_3$
FW:	503.6
Purity:	≥98%
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

XL888 is supplied as a crystalline solid. A stock solution may be made by dissolving the XL888 in the solvent of choice, which should be purged with an inert gas. XL888 is soluble in organic solvents such as DMSO and dimethyl formamide. The solubility of XL888 in these solvents is approximately 30 mg/ml.

XL888 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, XL888 should first be dissolved in DMSO and then diluted with the aqueous buffer of choice. XL888 has a solubility of approximately 0.1 mg/ml in a 1:5 solution of DMSO:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Description

Heat shock protein 90 (Hsp90) is a chaperone that maintains the functionality of client proteins involved in cell proliferation, cell cycling, and apoptosis.[1] XL888 is an ATP-competitive inhibitor of Hsp90.[2] Through this action, specific client proteins are degraded, resulting in cell cycle arrest or apoptosis.[3-5] XL888 is orally bioavailable and shows efficacy in tumor regression in gastric carcinoma and melanoma xenografts in mice.[2,4]

References

1. Taldone, T., Sun, W., and Chiosis, G. Discovery and development of heat shock protein 90 inhibitors. *Bioorg. Med. Chem.* **17(6)**, 2225-2235 (2009).
2. Bussenius, J., Blazey, C.M., Aay, N., *et al*. Discovery of XL888: A novel tropane-derived small molecule inhibitor of HSP90. *Bioorg. Med. Chem. Lett.* **22(17)**, 5396-5404 (2012).
3. Lyman, S.K., Crawley, S.C., Gong, R., *et al*. High-content, high-throughput analysis of cell cycle perturbations induced by the HSP90 inhibitor XL888. *PLoS One* **6(3)**, 1-14 (2011).
4. Haarberg, H.E., Paraiso, K.H.T., Wood, E., *et al*. Inhibition of Wee1, AKT, and CDK4 underlies the efficacy of the HSP90 inhibitor XL888 in an *in vivo* model of *NRAS*-mutant melanoma. *Mol. Cancer Ther.* **12(6)**, 901-912 (2013).
5. Paraiso, K.H.T., Haarberg, H.E., Wood, E., *et al*. The HSP90 inhibitor XL888 overcomes BRAF inhibitor resistance mediated through diverse mechanisms. *Clin. Cancer Res.* **18(9)**, 2502-2514 (2012).

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