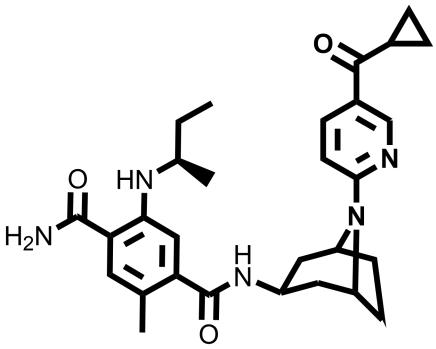
Xcess Biosciences Inc.
7144 N Harlem Ave #169
Chicago, IL 60631 USA

http://www.xcessbio.com
Toll free: 1-866-706-2330
Fax: 1-619- 810-0718
Email: info@xcessbio.com

HSP90 Inhibitor – XL888

Chemical Name: 5-((R)-sec-butylamino)-N1-((1R,3s,5S)-8-(5-(cyclopropanecarbonyl)pyridin-2-yl)-8-azabicyclo[3.2.1]octan-3-yl)-2-methylterephthalamide



Molecular Weight:	503.64
Formula:	$C_{29}H_{37}N_5O_3$
Purity:	≥98%
CAS#:	1149705-71-4
Solubility:	DMSO up to 100 mM
Storage	Powder: 4 °C 1 year DMSO: 4 °C 3 months -20 °C 1 year

Biological Activity:

XL888 is a highly potent, ATP-competitive and orally bioavailable small-molecule inhibitor of heat shock protein 90 (Hsp90) with antineoplastic activity. It specifically binds to Hsp90 with an IC_{50} of 24 nM. XL888 inhibits HSP90's chaperone function and promotes the proteasomal degradation of oncogenic signaling proteins involved in tumor cell proliferation and survival. In vivo XL888 significantly induces the regression of, or growth inhibition of established M229R and 1205LuR xenografts in SCID mice. XL888 treatment is noted to be proapoptotic in vivo and leads to increased TUNEL staining in M229R xenografts associated with increased expression of BIM and decreased expression of Mcl-1.

How to Use:

In vitro: XL888 was used at 10 μM in vitro and in cellular assays.

In vivo: XL888 was orally dosed to mice at 100 mg/kg 3 times a week in xenograft models

Reference:

1. Haarberg HE, 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. (2013) Mol Cancer Ther. 12(6):901-12.
2. Bussenius J, et al. Discovery of XL888: a novel tropane-derived small molecule inhibitor of HSP90. (2012) Bioorg Med Chem Lett. 22(17):5396-404.
3. Paraiso KH, et al. The HSP90 inhibitor XL888 overcomes BRAF inhibitor resistance mediated through diverse mechanisms.(2012) Clin Cancer Res. 18(9):2502-14.
4. Lyman SK, et al. High-content, high-throughput analysis of cell cycle perturbations induced by the HSP90 inhibitor XL888. (2011) PLoS One. 6(3):e17692.