Product Data Sheet

Product Name: SAR245409 (XL765)
Cat. No.: GC14884

Chemical Properties

Cas. No.	1349796-36-6		
Chemical Name	N-[4-[[3-(3,5-dimethoxyanilino)quinoxalin-2-yl]sulfamoyl]phenyl]-3-methoxy-4-methylbenzamide		
SMILES	CC1=C(C=C(C=C1)C(=O)NC2=CC=C(C=C2)S(=O)(=O)NC3=NC4=CC=CC=C4N=C3NC5=CC(=CC(=C5)OC)OC)OC		
Formula	$C_{31}H_{29}N_5O_6S$	M.Wt	599.66
Solubility	≥ 15mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	SAR245409 (XL765)		

Background

SAR245409 (XL765) is a selective dual inhibitor of PI3K and mTOR (IC50= 9 nM for PI3Kγ).

PI3K (phosphatidylinositol-4,5-bisphosphate 3-kinase) is a family of enzymes involved in cellular functions such as cell growth, proliferation, differentiation, motility, survival and intracellular trafficking, which in turn are involved in cancer. It plays a key role in PI3K/Akt/mTOR pathway.

In PA cell lines, combination of XL765 and TMZ blocked the cell growth and led to apoptosis [1]. In a variety of tumor cell lines that mutated on PI3K signaling, XL765 inhibited PIP3 formation in the membrane and AKT/p70S6K/S6 phosphorylation [2].

In GH3 xenograft tumor mouse models, combination use of XL765 and TMZ inhibited tumor growth, reduced serum GH and prolactin levels with no increased systemic side

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effects [1]. In severe combined immunodeficient mice, XL765 abolished MPNST local and metastatic growth. [3]. In multiple human xenograft models in nude mice, repeat dose administration showed significant tumor growth inhibition that related to antiproliferative and antiangiogenic response etc. [2]

References:

1. Dai C, Zhang B, Liu X et al. Inhibition of PI3K/AKT/mTOR pathway enhances temozolomide-induced cytotoxicity in pituitary adenoma cell lines in vitro and xenografted pituitary adenoma in female nude mice. Endocrinology. 2013 Mar;154(3):1247-59.
2. Yu P, Laird AD, Du X et al. Characterization of the activity of the PI3K/mTOR inhibitor XL765 (SAR245409) in tumor models with diverse genetic alterations affecting the PI3K pathway. Mol
Cancer Ther. 2014 May;13(5):1078-91.
3. Ghadimi MP, Lopez G, Torres KE et al. Targeting the PI3K/mTOR axis, alone and in combination with autophagy blockade, for the treatment of malignant peripheral nerve sheath tumors. Mol Cancer Ther. 2012 Aug;11(8):1758-69.