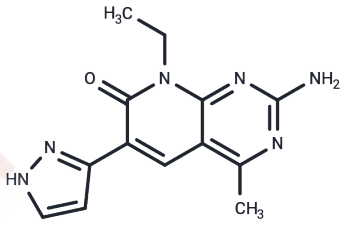
Data Sheet (Cat.No.T7014)

TargetMol

Voxtalisib

Chemical Properties



CAS No. : 934493-76-2

Formula: C13H14N6O

Molecular Weight: 270.29

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Voxtalisib (XL765) (SAR245409, XL765) is a dual inhibitor of mTOR/PI3K, mostly for p110γ with IC50 of 9 nM; also inhibits DNA-PK and mTOR. Phase 1/2.
Targets(IC50)	DNA-PK,mTOR,PI3K
In vitro	Voxtalisib is active against class I PI3K (IC50 = 39, 113, 9 and 43 nM for p110α, β, γ and δ, respectively). Voxtalisib also inhibits DNA-PK (IC50 = 150 nM) and mTOR (IC50 = 157 nM) but not XL-147 which shows IC50 values of > 15 μM. [1] Voxtalisib treatment results in decreased cell viability in 13 PDA cell lines in a dose-dependent manner. Voxtalisib, a dual-target PI3K/mTOR inhibitor, inhibits cell growth and apoptosis in many more cell lines and at lower concentrations as compared to the PI3K-selective inhibitors XL147 and PIK90. The effect can be recapitulated by using combinations of single-targeted compounds. Voxtalisib significantly reduces phosphorylation of the mTOR targets S6, S6K, and 4EBP1, which is associated with greater apoptosis induction rather than to PI3K inhibition alone. Voxtalisib treatment causes accumulation of autophagosomes in MIAPaCa-2 cells, and results in significant dose-dependent AVO induction and LC3-II stimulation in MIAPaCa-2 cells stably expressing a LC3-GFP construct. [2]
In vivo	The combination of Voxtalisib (30 mg/kg) with chloroquine (50 mg/kg) results in significant inhibition of BxPC-3 xenograft growth in mice models, while Voxtalisib alone at the same dose has no inhibitory effect. [2] Oral administration of Voxtalisib results in greater than 12-fold reduction in median tumor bioluminescence compared to control and improvement in median survival in nude mice implanted intracranially with GBM 39-luc cells. Voxtalisib in combination with temozolomide (TMZ) yields a 140-fold reduction in median bioluminescence with a trend toward improvement in median survival compared with TMZ alone. [3]
Cell Research	Cells are treated with XL765 24 hours after plating and harvested for apoptosis or autophagy assays at 24, 48, or 72 hours after XL765 treatment. Apoptosis is determined by total percentage of annexin V-positive cells by fluorescence-activated cell sorting (FACS). Acidic vesicular organelles (AVOs) are detected in XL765-treated cells by vital staining with acridine orange. The degree of AVO formation is expressed as fold increase of acridine orange fluorescence intensity (FL3) in XL765-treated cells versus control cells. (Only for Reference)

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 50 mg/mL (184.99 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 1 mg/mL (3.7 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.6997 mL	18.4986 mL	36.9973 mL
5 mM	0.7399 mL	3.6997 mL	7.3995 mL
10 mM	0.370 mL	1.8499 mL	3.6997 mL
50 mM	0.074 mL	0.370 mL	0.7399 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Garcia-Echeverria C, et al. Oncogene, 2008, 27(41), 5511-5526.
Mirzoeva OK, et al. J Mol Med, 2011, 89(9), 877-889.
Prasad G, et al. Neuro Oncol, 2011, 13(4), 384-392.