Product Data Sheet

Product Name: THZ1 2HCl
Cat. No.: GC25996

Chemical Properties

Cas. No.	2095433-94-4		
Formula	C31H30Cl3N7O2	M.Wt	638.97
Solubility	DMSO: 100 mg/mL (156.50 mM);Water: Insoluble;Ethanol: Insoluble	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	THZ1 2HCl		

Background

THZ1 is a covalent CDK7 inhibitor which has the unprecedented ability to target a remote cysteine residue located outside of the canonical kinase domain, providing an unanticipated means of achieving selectivity for CDK7.

THZ1 uses a unique mechanism, combining ATP-site and allosteric covalent binding, as a means of attaining potency and selectivity for CDK7. THZ1 irreversibly inhibits RNAPII CTD phosphorylation by covalently targeting a unique cysteine located outside the kinase domain of CDK7. THZ1, but not THZ1-R, completely inhibits the phosphorylation of the established intracellular CDK7 substrate RNAPII CTD at Ser 5 and Ser 7, with concurrent loss of Ser 2 phosphorylation at 250 nM in Jurkat cells. THZ1 exhibits strong antiproliferative effects across a broad range of cancer cell lines from various cancer types. In Jurkat cells, low-dose THZ1 has a profound effect on a small subset of genes, including the key regulator RUNX1, thus contributing to subsequent loss of the greater gene expression program and cell death[1]. THZ1 causes defects in Pol II(polymerase II) phosphorylation, co-transcriptional capping, promoter proximal pausing, and productive elongation[2].

THZ1 reduces the proliferation of KOPTK1 T-ALL cells in a human xenograft mouse

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model. THZ1 is well tolerated at 10 mg/kg with no observable body weight loss or behavioural changes, suggesting that it causes no overt toxicity in the animals[1].

[1] Kwiatkowski N, et al. Nature. 2014, 511(7511):616-20. [2] Nilson KA, et al. Mol Cell. 2015, 59(4):576-87.