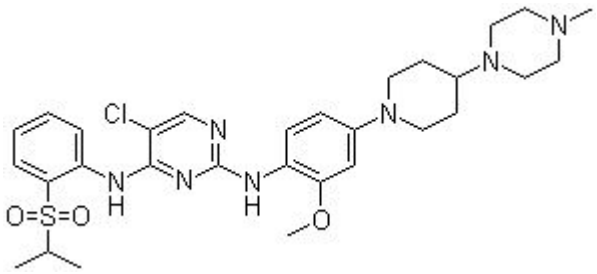
Product Introduction

TAE684 (NVP-TAE684)

TAE684 is a potent and selective **ALK** inhibitor with **IC50** of 3 nM, 100-fold more sensitive for ALK than InsR.

Technical Data:

Molecular Weight (MW):	614.2	
Formula:	$C_{30}H_{40}ClN_7O_3S$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 3 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	761439-42-3	

Biological Activity

TAE684 does not exhibit significant cross-reactivity against other kinases. TAE684 potently inhibits the proliferation of Ba/F3 NPM-ALK cells with IC50 of 3 nM, without affecting the survival of Ba/F3 cells even at 1 μM. TAE684 also inhibits proliferation of NPM-ALK-expressing human ALCL cell lines including Karpas-299 and SU-DHL-1 with IC50 of 2–5 nM. Molecular modeling reveals that L258 may be one of the major kinase-selectivity determinants for TAE684. TAE684 treatment results in a rapid and sustained inhibition of phosphorylation of NPM-ALK. TAE684 induces apoptosis and G1 phase arrest in NPM-ALK-expressing Ba/F3 cells and ALCL patient cell lines. [1] TAE684 markedly overcomes

Crizotinib-resistance in H3122 CR cells, harboring the fusion oncogene EML4-ALK, decreasing cell growth, suppressing ALK phosphorylation and inducing apoptosis.[2] Neurite outgrowth induced by expression of the mALK R1279Q mutant could be completely inhibited by TAE684 at 30 nM. [3]

After 4 weeks of treatment with TAE684 at 3 and 10 mg/kg, there is a significant delay in lymphoma development and 100- to 1,000-fold reduction in luminescence signal, without any signs of compound- or disease-related toxicity in Karpas-299 lymphoma model. TAE684 treatment also induces disease regression in established Karpas-299 lymphomas and down-regulates CD30 expression. [1] TAE684 also shows impressive antitumor activity against H3122 CR xenograft tumors. [2] Furthermore, treatment with TAE684 improves the rough eye phenotype of both ALK mutants, especially that seen with ALKR1275Q, whereas Crizotinib has little effect on either phenotype. [3]

References

[1] Galkin AV, et al. Proc Natl Acad Sci U S A, 2007, 104(1), 270-275.

[2] Katayama R, et al. Proc Natl Acad Sci U S A, 2011, 108(18), 7535-7540.

[3] Sch?nherr C, et al, Biochem J, 2011, 440(3), 405-413.