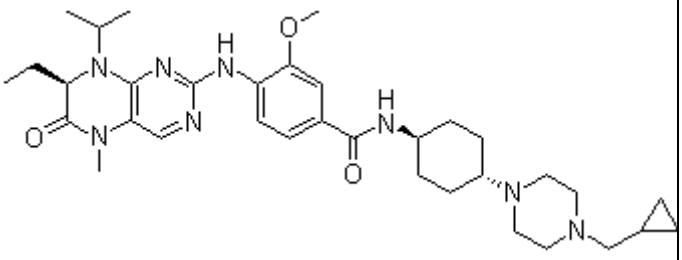
Product Introduction

Volasertib (BI 6727)

BI6727 (Volasertib) is a highly potent Plk1 **inhibitor with** IC50 **of 0.87 nM. It shows 6- and 65-fold greater selectivity against Plk2 and Plk3. Phase 2.**

Technical Data:

Molecular Weight (MW):	618.81	
Formula:	$C_{34}H_{50}N_8O_3$	
Solubility (25 ℃) * <1 mg/ml means slightly soluble or insoluble:	DMSO 50 mg/mL	
	Water <1 mg/mL	
	Ethanol 124 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	755038-65-4	

Biological Activity

Like BI2536, BI6727 is an ATP-competitive kinase inhibitor from the dihydropteridinone class of compounds. In addition to Plk1, BI6727 also potently inhibits two closely related kinases Plk2 and Plk3 with IC50 of 5 nM and 56 nM, respectively. BI6727 at concentrations up to 10 μM displays no inhibitory activity against a panel of >50 other kinases. BI6727 inhibits the proliferation of multiple cell lines derived from various cancer tissues, including HCT116, NCI-H460, BRO, GRANTA-519, HL-60, THP-1, and Raji cells with EC50 of 23 nM, 21 nM, 11 nM, 15 nM, 32 nM, 36 nM, and 37 nM, respectively. BI6727 treatment (100 nM) in NCI-H460 cells induces an accumulation of mitotic cells with monopolar spindles and positive

staining for histone H3 phosphoserine 10, confirming that cells are arrested early in the M phase, followed by induction of apoptosis. [1] Low nanomolar concentrations of BI6727 display potent inhibitory activity against neuroblastoma (NB) tumor-initiating cells (NB TIC) with EC50 of 21 nM, whereas only micromolar concentrations of BI6727 are cytotoxic for normal pediatric neural stem cells. [2]BI6727 induces growth arrest of Daoy and ONS-76 medulloblastoma cells similar to BI 2536. [3]

Administration of BI6727 significantly inhibits the growth of multiple human carcinoma xenografts including HCT116, NCI-H460, and taxane-resistant CXB1 colon carcinoma, accompanied by an increase in the mitotic index as well as an increase in apoptosis. [1] In in vivo studies, BI6727 shows better toxicity and pharmacokinetic profile compared to BI2536. [3]

A high volume of distribution, indicating good tissue penetration, and a long terminal half-life.

References

[1] Rudolph D, et al. Clin Cancer Res, 2009, 15(9), 3094-3102.

[2] Grinshtein N, et al. Cancer Res, 2011, 71(4), 1385-1395.

[3] Harris PS, et al. BMC Cancer, 2012, 12, 80.

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