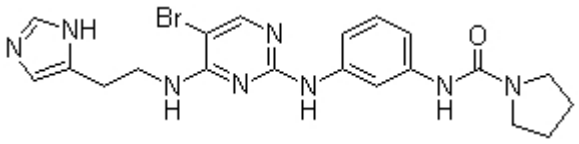
Product Introduction

BX-912

BX912 is a potent and specific **PDK1** inhibitor with **IC50** of 12 nM, 9- and 105- fold greater selectivity for PDK1 than PKA and PKC, respectively. In comparison to GSK3β, selectivity for PDK1 is 600-fold.

Technical Data:

Molecular Weight (MW):	471.35	
Formula:	$C_{20}H_{23}BrN_8O$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 94 mg/mL	
	Water <1 mg/mL	
	Ethanol 94 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	702674-56-4	

Biological Activity

BX912 prevents ChcK1, PKA, c-kit, and KDR with IC50 of 0.83, 0.11, 0.85, and 0.41 μM, resepectively. BX912 blocks PDK1/Akt signaling in tumor cells and suppresses the anchorage-dependent growth of a variety of tumor cell lines (such as PC-3 cells) in culture or induces apoptosis. A number of cancer cell lines (such as MDA-468 breast cancer) with elevated Akt activity are >30-fold more sensitive to growth inhibition by PDK1 inhibitor BX912 in soft agar than on tissue culture plastic, consistent with the cell survival function of the PDK1/Akt signaling pathway, which is particularly important for unattached cells.

BX912 potently blocks PDK1 enzyme activity in a direct kinase assay format, although BX912 fails to block preactivated AKT2 activity (IC50 > 10 μM). Therefore, BX-912 is a direct inhibitor of PDK1. BX912 is a competitive inhibitor of PDK1 activity with respect to its substrate, ATP, suggesting that BX912 binds to the ATP binding pocket of PDK1. The aminopyrimidine backbone of BX912 adopts a similar orientation in the active site of PDK1. BX912 promotes a pronounced increase in the population of MDA-468 cells with 4 N DNA content, indicative of a block at the G2/M phase of the cell cycle. BX912 also potently inhibits the growth of HCT-116 cells in soft agar, showing a 96% inhibitory effect at a dose of 1 μM. BX912 potently inhibits the growth of PC-3 cells in soft agar, displaying IC50 of 0.32 μM. [1]

References

[1] Feldman RI, et al. J Biol Chem. 2005, 280(20), 19867-19874.

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