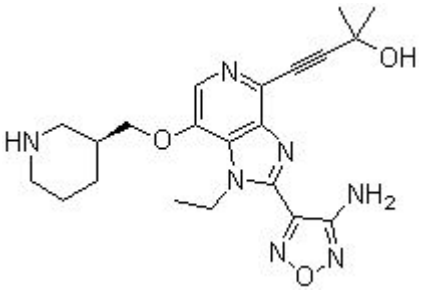
Product Introduction

GSK690693

GSK690693 is a pan-Akt inhibitor targeting **Akt1/2/3** with **IC50** of 2 nM/13 nM/9 nM, also sensitive to the AGC kinase family: PKA, PrkX and PKC isozymes. Phase 1.

Technical Data:

Molecular Weight (MW):	425.48	
Formula:	C21H27N7O3	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 39 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	937174-76-0	

Biological Activity

GSK690693 is very selective for the Akt isoforms versus the majority of kinases in other families. However, GSK690693 is less selective for members of the AGC kinase family including PKA, PrkX, and PKC isozymes with IC50 of 24 nM, 5 nM, and 2-21 nM, respectively. GSK690693 also potently inhibits AMPK and DAPK3 from the CAMK family with IC50 of 50 nM and 81 nM, respectively, and PAK4, 5, and 6 from the STE family with IC50 of 10 nM, 52 nM, and 6 nM, respectively. GSK690693 inhibits the phosphorylation of GSK3β in tumor cells with IC50 ranging from 43 nM to 150 nM. GSK690693 treatment leads to a dose-dependent

increase in the nuclear accumulation of the transcription factor FOXO3A. GSK690693 potently inhibits the proliferation of T47D, ZR-75-1, BT474, HCC1954, MDA-MB-453, and LNCaP cells with IC50 of 72 nM, 79 nM, 86 nM, 119 nM, 975 nM, and 147 nM, respectively. GSK690693 treatment induces apoptosis at concentrations >100 nM in both LNCaP and BT474 cells. [1] Consistent with the role of AKT in cell survival, GSK690693 induces apoptosis in sensitive ALL cell lines. [2]

A single administration of GSK690693 inhibits GSK3β phosphorylation in human breast carcinoma (BT474) xenografts in a dose- and time-dependent manner. Similarly, GSK690693 induces a reduction in phosphorylation of the Akt substrates, PRAS40, and FKHR/FKHRL1. GSK690693 also results in an acute increase in blood glucose, returning to baseline 8 to 10 hours after drug administration. Administration of GSK690693 induces reductions in phosphorylated Akt substrates in vivo, and potently inhibits the growth of human SKOV-3 ovarian, LNCaP prostate, and BT474 and HCC-1954 breast carcinoma xenografts, with maximal inhibition of 58% to 75% at the dose of 30 mg/kg/day. [1] GSK690693 exhibits efficacy irrespective of the mechanism of Akt activation involved. GSK690693 is most effective in delaying tumor progression in Lck-MyrAkt2 mice expressing a membrane-bound, constitutively active form of Akt. [3]

References

[1] Rhodes N, et al. Cancer Res, 2008, 68(7), 2366-2374.
[2] Levy DS, et al. Blood, 2009, 113(8), 1723-1729.
[3] Altomare DA, et al. Clin Cancer Res, 2010, 16(2), 486-496.

Note： Products protected by valid patents are not offered for sale in countries where the sale of such products constitutes a patent infringement and its liability is at buyer’s risk. This item is only for R&D purpose not for commercial business in kilos. Buyers should overview the patent issue in their countries.