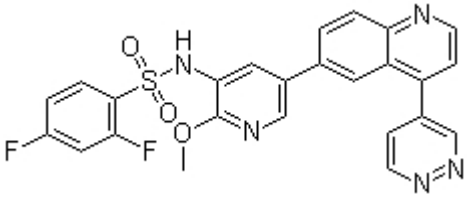
Product Introduction

GSK2126458 (GSK458)

GSK2126458 is a highly selective and potent inhibitor of **p110α/β/δ/γ**, mTORC1/2 with K_I of 0.019 nM/0.13 nM/0.024 nM/0.06 nM and 0.18 nM/0.3 nM, respectively. Phase 1.

Technical Data:

Molecular Weight (MW):	505.5	
Formula:	$C_{25}H_{17}F_2N_5O_3S$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 100 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	1086062-66-9	

Biological Activity

GSK2126458 potently inhibits the activity of common activating mutants of p110α (E542K, E545K, and H1047R) found in human cancer with K_i of 8 pM, 8 pM and 9 pM, respectively. [1] GSK2126458 causes a significant reduction in the levels of pAkt-S473 with remarkable potency in T47D and BT474 cells with IC50 of 0.41 nM and 0.18 nM, respectively. Furthermore, GSK2126458 leads to a G1 cell cycle arrest and produces the inhibitory effect on cell proliferation in a large panel of cell lines, including T47D and BT474 breast cancer lines with IC50 of 3 nM and 2.4 nM, respectively. [1]

In a BT474 human tumor xenograft model, GSK2126458 treatment results in a dose-dependent reduction in pAkt-S473 levels, and exhibited dose-dependent tumor growth inhibition at a low dose of 300 μg /kg. Besides, GSK2126458 shows low blood clearance and good oral bioavailability in four preclinical species (mouse, rat, dog, and monkey). [1]

References

[1] Knight SD, et al. ACS Med. Chem. Lett. 2010, 1 (1), 39–43.

[2] Greger JG, et al. Mol Cancer Ther. 2012, 11(4), 909-920.