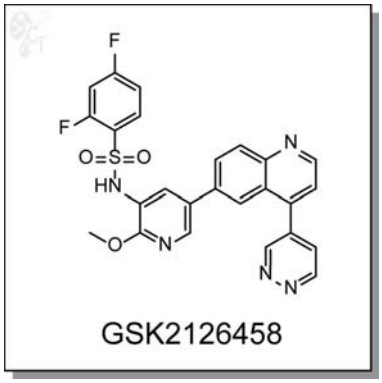
Product Specification Sheet

Product Name: GSK2126458

Catalog Number: C4212



Technical information:

Chemical Formula:	$C_{25}H_{17}F_2N_5O_3S$
CAS #:	1086062-66-9
Molecular Weight:	505.5
Purity:	> 98%
Appearance:	White solid
Solubility:	Soluble in DMSO up to 100mM
Chemical Name:	2,4-difluoro-N-(2-methoxy-5-(4-(pyridazin-4-yl)quinolin-6-yl)pyridin-3-yl)benzenesulfonamide
Storage:	Store solid powder at 4°C desiccated; Store DMSO solution at -20°C.
Shelf Life:	In the unopened package, powder is stable for 1 year and DMSO solution is stable for 6 months under proper storage condition.

Handling:

- To make 10 mM stock solution, add 0.198mL of DMSO for each mg of GSK2126458
- For DMSO solution, briefly spin the vial at 500 rpm in a 50 mL conical tube to ensure maximum sample recovery.

Biological Activity:

GSK2126458 is an orally available, pyridazine-quinoline-based inhibitor of of p110α, p110β, p110γ, p110δ, mTORC1, and mTORC2 with Ki of 0.019 nM, 0.13 nM, 0.024 nM, 0.06 nM, 0.18 nM and 0.3 nM, respectively. [1] In mechanistic assays, GSK2126458 induced significant reduction in levels of pAKT-S473 (0.41 nM in T47D and 0.18 nM in BT474). It also inhibits phosphorylation of AKT-T308 and p70S6K at low nanomolar concentrations. Induction of caspase 3 and 7 activity suggests that GSK2126458 utilizes apoptosis as a mechanism for cell death. [2]

Combination of GSK2126458 with B-Raf inhibitor GSK2118436 (Dabrafenib) enhanced cell growth inhibition and decreased S6 ribosomal protein phosphorylation in NRAS and MEK mutant clones. Combination of GSK2126458 and MEK inhibitor GSK1120212 (trametinib) has been studied in Phase I clinical trials. [3]

Reference:

1. Knight et al., ACS Med. Chem. Lett. 2010, 1, 39-43.
2. Hardwick et al., Mol. Cancer Ther. 2009, 8(12), Supplement I, Abstract C63.
3. Greger et al., Combinations of BRAF, MEK, and PI3K/mTOR inhibitors overcome acquired resistance to the BRAF inhibitor GSK2118436 dabrafenib, mediated by NRAS or MEK mutations. Mol. Cancer Ther. 2012, 11(4), 909-920. Pubmed ID: 22389471

To reorder: http://www.cellagentech.com/GSK2126458/

For Technical Support: technical@cellagentech.com

Chemicals are sold for research use only, not for clinical or diagnostic use.