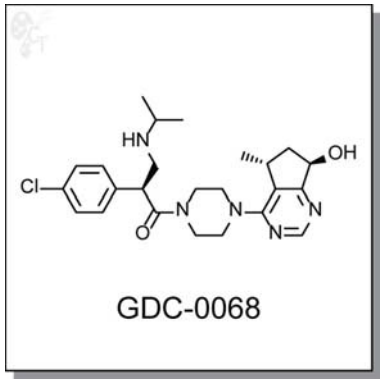
Product Specification Sheet

Product Name: GDC-0068

Catalog Number: C4006



GDC-0068

Technical information:

Chemical Formula:	$C_{24}H_{32}ClN_5O_2$
CAS #:	1001264-89-6
Molecular Weight:	458
Purity:	> 98%
Appearance:	White
Solubility:	Soluble in DMSO up to 100 mM
Chemical Name:	(S)-2-(4-chlorophenyl)-1-(4-((5R,7R)-7-hydroxy-5-methyl-6,7-dihydro-5H-cyclopenta[d]pyrimidin-4-yl)piperazin-1-yl)-3-(isopropylamino)propan-1-one
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 0.218mL of DMSO for each mg of GDC-0068
- For DMSO solution, briefly spin the vial at 500 rpm in a 50 mL conical tube to ensure maximum sample recovery.

Biological Activity:

GDC-0068 is a potent, highly selective, orally available, ATP-competitive pan-AKT inhibitor, targeting Akt1, Akt2 and Akt3 with IC50 of 5 nM, 18 nM and 8 nM, respectively. It demonstrates high selectivity
over more than 200 screened kinases, with >100 fold selectivity for Akt over PKA [1-4].

Akt functions as a central role of the PI3K-Akt-mTOR pathway. It is one of the most frequently activated protein serine/threonine kinases in human malignancies. Inhibiting Akt activity has become an attractive approach for cancer treatment. GDC-0068 blocks the phosphorylation of multiple downstream targets of Akt in human cancer cell lines in a dose-dependent manner. It inhibits cell cycle progression and viability of cancer cell lines, most robustly in cells with activated PI3K-Akt-mTOR pathway driven by PIK3CA , PTEN loss and HER2 amplification. GDC-0068 treatment results in pronounced PD effects in tumor xenograft models including dose dependent suppression of p-PRAS40, P-S6 and P-eIF4G, as well as induction of FOXO nuclear localization. GDC-0086 has exhibited antitumor efficacy in multiple xenograft tumor models. In addition, consistent with the role of Akt in a survival pathway, GDC-0068 also demonstrates enhanced antitumor efficacy when combined with other therapeutic agents. GDC-0068 is currently in Phase 1a and Phase 1b clinical development in cancer patients [1-4].

Reference:

1. Blake JF, et al. Discovery and Preclinical Pharmacology of a Selective ATP-Competitive Akt Inhibitor (GDC-0068) for the Treatment of Human Tumors. J Med Chem. 2012. 55(18):8110-27. Pubmed ID: 22934575
2. Lin K. GDC-0068: A novel, selective, ATP-competitive inhibitor of Akt. Cancer Res, 2011, 71(8 Supplement), abstract DDT02-01.
3. Blake JF. Discovery of GDC-0068: A Selective ATP-competitive Akt Inhibitor for the Treatment of Human Tumors. CHI Next Generation Kinase Inhibitors. June 6-8, 2011. http://www.arraybiopharma.com/ documents/Publication/PubAttachment478.pdf
4. Abernero J, et al. Targeting the PI3K-Akt-mTOR pathway with GDC-0068, a novel selective ATP competitive Akt inhibitor. http://www.arraybiopharma.com/_documents/Publication/PubAttachment437.pdf

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