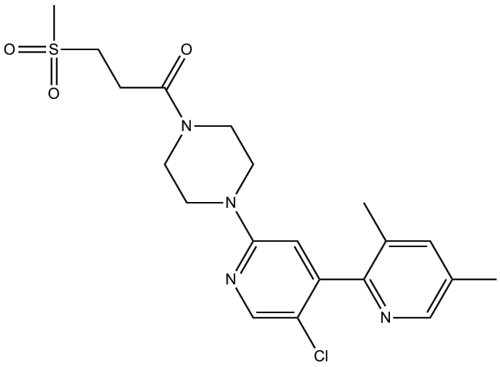
Product Data Sheet

Product Name: PF-5274857
Cat. No.: GC13280

Chemical Properties

Cas. No.	1373615-35-0		
Chemical Name	1-[4-[5-chloro-4-(3,5-dimethylpyridin-2-yl)pyridin-2-yl]piperazin-1-yl]-3-methylsulfonylpropan-1-one		
SMILES	CC1=CC(=C(N=C1)C2=CC(=NC=C2Cl)N3CCN(CC3)C(=O)CCS(=O)(=O)C)C		
Formula	$C_{20}H_{25}ClN_4O_3S$	M.Wt	436.96
Solubility	≥ 19.65mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Background

PF-5274857 is an inhibitor of hedgehog (Hh) signaling pathway and is identified as a potent and selective antagonist of Smoothened (Smo) with an IC50 of 5.8 nM.

Smoothened, a G protein-coupled receptor, is a component of the hedgehog signaling pathway and is conserved from flies to humans. This protein is the molecular target of the teratogen cyclopamine. SMO can act as an oncogene and the activation of SMO mutations leads to unregulated activation of the hedgehog pathway and cancer.

Caution: Product has not been fully validated for medical applications. For research use only.
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In MEF cells, treatment of PF-5274857 completely blocked Shh-induced Hh pathway activity, which was measured by the transcriptional activity of Smo downstream gene Gli1.

In vivo, PF-5274857 showed anti-tumor activity in a mouse medulloblastoma model with IC50 of 8.9 nM. PF-5274857 also shows significant dose-dependent tumor growth inhibition (TGI) and induces tumor regression. In skin tissue, downregulation of Gli1 and Gli2 is also observed with a similar time course by PF-52748571.

Reference:

1. Rohner A, Spilker ME, Lam JL, et al. Effective targeting of Hedgehog signaling in a medulloblastoma model with PF-5274857, a potent and selective Smoothened antagonist that penetrates the blood-brain barrier. Molecular cancer therapeutics.2012;11(1):57-65.

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