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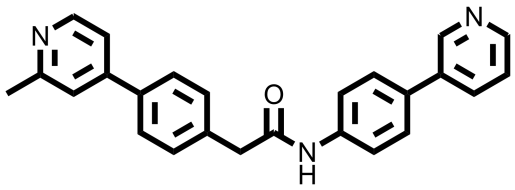
Wnt Antagonist Wnt-C59

Chemical Name: 2-(4-(2-methylpyridin-4-yl)phenyl)-N-(4-(pyridin-3-yl)phenyl)acetamide



Molecular Weight:	379.45
Formula:	$C_{25}H_{21}N_3O$
Purity:	≥98%
CAS#:	1243243-89-1
Solubility:	DMSO up to 50 mM
Storage	Powder: 4°C 1 year DMSO: 4°C 3 month -20°C 1 year

Biological Activity:

Wnt-C59 is a very potent and highly selective Wnt signaling antagonist with an IC_{50} ~ 74 pM in the Wnt signaling reporter assay. It prevents palmitylation of Wnt proteins by Porcupine (a membrane-bound O-acyltransferase), thereby blocking Wnt protein secretion and activity. Wnt-C59 displayed good bioavailability as once daily oral administration and blocked progression of mammary tumors in MMTV-WNT1 transgenic mice model while downregulating Wnt/β-catenin target genes. Because Wnt-C59 exhibits much better potency and selectivity than the reported IWP series of Porcupine/Wnt inhibitors, it serves as the better Wnt pathway inhibitor for in vitro and in vivo studies.

How to Use:

In vitro: Wnt-C59 was used at 0.1-0.2 μM to completely block Wnt protein secretion. When used at 0.5 μM, it can be used functionally replace the Dkk protein in many assay conditions

In vivo: Wnt-C59 was used to dose mice orally at 5-10 mg/kg once per day or 5 mg/kg twice per day.

Reference:

1. Proffitt KD, et al. Pharmacological inhibition of the Wnt acyltransferase PORCN prevents growth of WNT-driven mammary cancer. (2013) Cancer Res. 15;73(2):502-7.
2. Chen D, et al. (N-(HETERO)ARYL,2-(HETERO)ARYL-SUBSTITUTED ACETAMIDES FOR USE AS WNT SIGNALING MODULATORS. PCT WO/2010/101849.
3. Chen B, et al. Small molecule-mediated disruption of Wnt-dependent signaling in tissue regeneration and cancer. (2009) Nat Chem Biol. 5(2):100-7.
4. Dodge ME, et al. Diverse chemical scaffolds support direct inhibition of the membrane bound O-acyltransferase Porcupine. (2012) J Biol Chem. 287 (27), pp. 23246–23254
5. Willems E, et al. Small-molecule inhibitors of the Wnt pathway potently promote cardiomyocytes from human embryonic stem cell-derived mesoderm. (2011) Circ Res.109(4):360-4.