For Research Use Only

VPS34 inhibitor 1 (Compound 19, PIK-III analogue)

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Catalog Number: CM14279

产品信息

Catalog Number:
CM14279

CAS号:
1383716-46-8

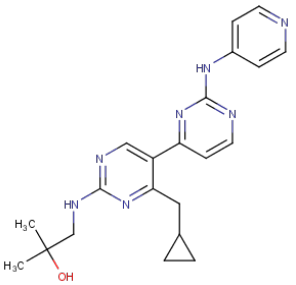
分子式:
$C_{21}H_{25}N_7O$

主要靶点:
PI3K

主要通路:
PI3K/Akt/mTOR信号通路

分子量:
391.47

溶解度:
DMSO:78 mg/mL (199.25 mM)



靶点活性

Vps34:15 nM

体外活性

VPS34 inhibitor 1 (Compound 19, PIK-III analogue) is extraordinarily selective over other lipid and protein kinases. The ability of compound 19 to prevent the degradation of autophagy substrates p62, NCOA4, NBR1, NDP52, and FTH1 is similar to PIK-III. In addition, treatment of cells with compound 19 leads to an increase in the lipidated and nonlipidated forms of LC3 similar to previous reports using PIK-III.

体内活性

The pharmacokinetic profile of analogue 19 is determined in C57BL/6 mice.?After oral administration at 10 mg/kg, the compound is rapidly absorbed and showed moderate mean systemic clearance (30 mL/min/kg, approximately 33% of hepatic blood flow), with good oral bioavailability (F% = 47).?Based on these PK parameters and the cellular activity, compound 19 constitutes a suitable candidate for in vivo studies.?Upon oral administration of compound 19 at 50 mg/kg twice a day (BID) for 7 days, LC3-II accumulates consistent with reduced autophagic capacity in time-dependent manner.?It inhibits autophagy in vivo.

动物实验

Animal Models: C57BL/6 Mice. Formulation: PG (20% v/v). Dosages: 10 mg/kg(p.o.) or 2 mg/kg(I.V.) .Administration: oral administration or I.V.

细胞实验

Cell lines: U2OS cells.Concentrations: 0, 1, 5, 10 μM. Incubation Time: 24 h .Method: For inhibitor assay, cells are plated and the following day when cells had reached 90%, are treated with dimethyl sulfoxide (DMSO, vehicle) or the indicated concentration of PIK-III or Compound 19, both dissolved in DMSO. 24 hours later, cells are lysed in RIPA supplemented with 1% SDS and mini-EDTA protease inhibitors, homogenized by passage through a Qiashredder column and the protein is quantified by DC Lowry protein assay.

描述

VPS34 inhibitor 1 (Compound 19, PIK-III analogue) is a potent and selective inhibitor of VPS34(IC50 : 15 nM)

储存

Powder: -20°C for 3 years | In solvent: -80°C for 2 years