

Product Data Sheet

Product Name: FLT3-IN-3

Cat. No.: GC19772

Chemical Properties

Cas. No. 2229050-90-0

SMILES N[C@H](CC1)CC[C@@H]1NC2=NC3=C(N=CN3C4CCCC4)C(NC5=CC=C(CN6CCOCC6)C=C5)=N2

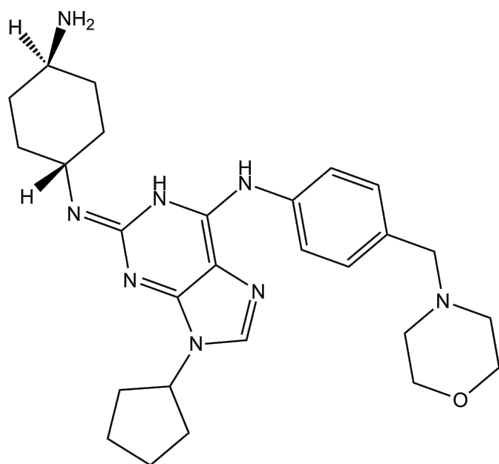
Formula $C_{27}H_{38}N_8O$ M.Wt 490.64

Solubility DMSO : 250 mg/mL (509.54 mM) 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

FLT3-IN-3 is a potent FLT3 inhibitor with IC50s of 13 and 8 nM for FLT3 WT and FLT3 D835Y, respectively.

FLT3-IN-3 (Compound 7d) inhibits the proliferation of FLT3-ITD positive MV4-11 and MOLM-13 cell lines very effectively at low nanomolar concentrations (GI50 values 2 and 1 nM, respectively)[1].

Caution: Product has not been fully validated for medical applications. For research use only.

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FLT3-IN-3 (1 nM, 10nM, 100 nM, 1 μ M and 10 μ M; 72 hours) inhibits the Ba/F3 FLT3-ITD cells with the GI50 of 0.034 ± 0.015 μ M, and inhibits the parental Ba/F3 cells with the GI50 value of 1.136 ± 0.389 μ M[1].

Concentrations as low as 1 nM are sufficient to block the autophosphorylation of the FLT3 receptor tyrosine kinase at three different tyrosine residues (589, 591, and 842). Moreover, this inhibition suppresses phosphorylation of several downstream targets of FLT3. Notably, FLT3-IN-3 (0.01, 0.1, 1, 10 and 100 nM; 1 hours) abolishes phosphorylation of STAT5 at Y694, which is a direct substrate of the oncogenic FLT3-ITD variant. The second pathway affected is the MAPK cascade: Two key components of this signaling pathway, ERK1/2 (T202/Y204) and MEK1/2 (S217/221), exhibit reduced phosphorylation upon treatment with FLT3-IN-3. FLT3-IN-3 also interferes with PI3K/AKT pathway which is confirmed by reduced phosphorylation of AKT at S473[1]

A single dose of FLT3-IN-3 (Compound 7d; 10 mg/kg; i.p.) in mice with subcutaneous MV4-11 xenografts causes sustained inhibition of FLT3 and STAT5 phosphorylation over 48 hours[1].

Reference:

[1]. Gucký T, et al. Discovery of N2-(4-Amino-cyclohexyl)-9-cyclopentyl- N6-(4-morpholin-4-ylmethyl-phenyl)- 9H-purine-2,6-diamine as a Potent FLT3 Kinase Inhibitor for Acute Myeloid Leukemia with FLT3 Mutations. J Med Chem. 2018 May 10;61(9):3855-3869.

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