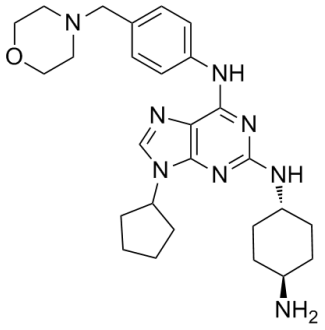
FLT3-IN-3

Cat. No.:	HY-112145
CAS No.:	2229050-90-0
Molecular Formula:	$C_{27}H_{38}N_8O$
Molecular Weight:	490.64
Target:	FLT3
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	Please store the product under the recommended conditions in the COA.



BIOLOGICAL ACTIVITY

Description	FLT3-IN-3 is a potent **FLT3** inhibitor with **IC_{50}**s of 13 and 8 nM for **FLT3 WT** and **FLT3 D835Y**, respectively.
IC_{50} & Target	IC50: 13 nM (FLT3 WT), 8 nM (FLT3 D835Y)[1]

In Vitro

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 (GI_{50} values 2 and 1 nM, respectively)[1].

FLT3-IN-3 (1 nM, 10nM, 100 nM, 1 μM and 10 μM; 72 hours) inhibits the Ba/F3 FLT3-ITD cells with the GI_{50} of 0.034±0.015 μM, and inhibits the parental Ba/F3 cells with the GI_{50} value of 1.136±0.389 μM[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 interfers with PI3K/AKT pathway which is confirmed by reduced phosphorylation of AKT at S473[1].

Cell Proliferation Assay[1]

Cell Line:	Murine Ba/F3 FLT3-ITD and parental Ba/F3 cells
Concentration:	1 nM, 10nM, 100 nM, 1 μM and 10 μM
Incubation Time:	72 hours
Result:	The GI_{50}s for Ba/F3 FLT3-ITD cells and parental Ba/F3 cells are 0.034±0.015 μM and 1.136±0.389 μM, respectively.

Western Blot Analysis[1]

Cell Line:	MV4-11 cells
Concentration:	0.01, 0.1, 1, 10 and 100 nM
Incubation Time:	1 hours

	Result:	Concentrations as low as 1 nM were sufficient to block the autophosphorylation of the FLT3 receptor tyrosine kinase at three different tyrosine residues (589, 591, and 842).
In Vivo	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].	
	Animal Model:	Female athymic nu/nu mice with subcutaneously implanted MV4-11 xenografts[1]
	Dosage:	10 mg/kg
	Administration:	Intraperitoneal (i.p.) injection; 48 hours
	Result:	Effectively inhibited FLT3-ITD autophosphorylation in MV4-11 xenografts.

REFERENCES

[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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