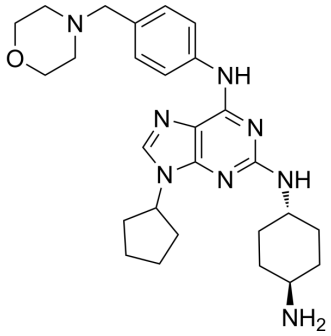
# FLT3-IN-3



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| **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:** | Powder -20°C 3 years<br>4°C 2 years<br>In solvent -80°C 6 months<br>-20°C 1 month |

## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 250 mg/mL (509.54 mM; Need ultrasonic)

| Preparing Stock Solutions | Solvent / Mass / Concentration | 1 mg | 5 mg | 10 mg |
|---|---|---|---|---|
| | 1 mM | 2.0382 mL | 10.1908 mL | 20.3815 mL |
| | 5 mM | 0.4076 mL | 2.0382 mL | 4.0763 mL |
| | 10 mM | 0.2038 mL | 1.0191 mL | 2.0382 mL |

Please refer to the solubility information to select the appropriate solvent.

**In Vivo**

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.24 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.24 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.24 mM); Clear solution

## BIOLOGICAL ACTIVITY

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| **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].<br>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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

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| 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]

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| 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].

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| 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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