# FLT3-IN-15

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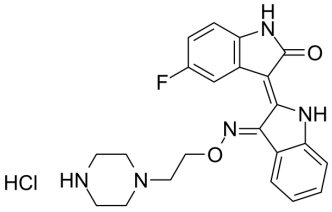
| **Cat. No.:** | HY-146886 |
| **CAS No.:** | 2435562-99-3 |
| **Molecular Formula:** | $C_{22}H_{23}ClFN_5O_2$ |
| **Molecular Weight:** | 443.9 |
| **Target:** | FLT3 |
| **Pathway:** | Protein Tyrosine Kinase/RTK |
| **Storage:** | Please store the product under the recommended conditions in the Certificate of Analysis. |




## BIOLOGICAL ACTIVITY

**Description**

FLT3-IN-15 is a highly potent and orally active FLT3 inhibitor with $IC_{50}$s of 0.87 nM and 0.32 nM for FLT3 and FLT3/D835Y, respectively. FLT3-IN-15 can be used for researching acute myeloid leukemia[1].

**$IC_{50}$ & Target**

$IC_{50}$: 0.87 nM (FLT3), 0.32 nM (FLT3/D835Y)[1]

**In Vitro**

FLT3-IN-15 (compound 36) (0-100 nM) exhibits anti-proliferative activities against MOLM14 cell lines[1].
FLT3-IN-15 (0-1 μM; 72 hours) shows extremely more sensitive against MV4-11 cells than K562 cell line, and displayed good safety profiles against other cancer cell lines[1].
FLT3-IN-15 (0.01-1 μM; 4 hours) shows strongly blockage of the phosphorylation of STAT5 and Erk1/2 in MV4-11 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay

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| Cell Line: | MOLM14 wild type cells, MOLM14-ITD cells, MOLM14-ITD-D835Y cells, MOLM14-ITD-F691L cells[1] |
| Concentration: | 0-100 nM |
| Incubation Time: | |
| Result: | Exhibited anti-proliferative activities against MOLM14 cell lines, with $GI_{50}$s of 4.88 ± 0.67 nM, 1.85 ± 0.06 nM, 1.87 ± 0.36 nM and 3.27 ± 0.99 nM in MOLM14 wild type cells, MOLM14-ITD cells, MOLM14-ITD-D835Y cells and MOLM14-ITD-F691L cells, respectively. |

Cell Proliferation Assay

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| Cell Line: | MV4-11, K562, A549, HepG2, MDA-MB-231, HCT-116, PC3 and SK-OV-3[1] |
| Concentration: | 0-1 μM |
| Incubation Time: | 72 hours |
| Result: | Showed extremely more sensitive against MV4-11 cells ($GI_{50}$ = 1 nM) than K562 cell line, and displayed good safety profiles against other cancer cell lines. |

Western Blot Analysis

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| Cell Line: | MV4-11[1] |
| Concentration: | 10 nM, 100 nM and 1 μM |
| Incubation Time: | 4 hours |
| Result: | Showed strongly blockage of the phosphorylation of STAT5 and Erk1/2. |

**In Vivo**

FLT3-IN-15 (20 mg/kg; PO; daily, for 21 days) results in the rapid and complete remission of tumors in all mice[1].
FLT3-IN-15 (2000 mg/kg; PO; single) causes one female mouse died at day 6, and the $LD_{50}$ value is calculated as 4,950 mg/kg in female mice[1].
FLT3-IN-15 (10 μM) shows 21.4% inhibition of hERG ligand binding[1].
FLT3-IN-15 (10 mg/kg; PO and IV; single) exhibits an $AUC_{last}$ of 25.0 μg·min/mL, a $C_{max}$ of 36.5 ng/mL, and a remarkable increase in the oral bioavailability of 42.6%[1].
Pharmacokinetic Parameters of FLT3-IN-15 in male ICR mice[1].

| | PO (10 mg/kg) | IV (10 mg/kg) |
|---|---|---|
| $AUC_{last}$ (μg·min/mL) | 25.0 ± 11.6 | 58.5 ± 57.4 |
| $AUC_{inf}$ (μg·min/mL) | 62.1 ± 58.6 | 103.4 ± 95.3 |
| MRT (hr) | 2811.3 ± 2713.0 | 1257.1 ± 1084.1 |
| $T_{1/2}$ (hr) | 1775.7 ± 1901.0 | 1099.2 ± 945.8 |
| CL (mL/min/kg) | | 158.7 ± 98.7 |
| $V_{SS}$ (L/kg) | | 127891 ± 104764 |
| $C_{max}$ (ng/mL) | 36.5 ± 24.3 | |
| $T_{max}$ (min) | 390.0 ± 366.0 | |
| Xu, 24h (%) | 0.001 ± 0.0 | 0.002 ± 0.002 |
| GI24h (%) | 0.05 ± 0.05 | 0.24 ± 0.02 |
| F (%) | 42.9 | |

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

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| Animal Model: | BALB/c nu/nu (injected with MV4-11)[1] |
| Dosage: | 20 mg/kg |
| Administration: | PO; daily, for 21 days |
| Result: | Resulted in the rapid and complete remission of tumors in all mice, and no weight loss or any other signs of toxicity during the administration period. |

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| Animal Model: | Female ICR mice[1] |
| Dosage: | 2000 mg/kg |
| Administration: | PO; single |
| Result: | Caused one female mouse of the 2,000 mg/kg group died at day 6 and the approximate lethal dose (ALD) is determined over 2,000 mg/kg in male mice and 2,000 mg/kg in female mice, respectively; the $LD_{50}$ value was calculated as 4,950 mg/kg in female mice. |

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|---|---|
| Animal Model: | Male ICR mice[1] |
| Dosage: | 10 mg/kg |
| Administration: | PO and IV; single (Pharmacokinetics Analysis) |
| Result: | Exhibited an $AUC_{last}$ of 25.0 μg·min/mL, a $C_{max}$ of 36.5 ng/mL, and a remarkable increase in the oral bioavailability of 42.6%. |

## REFERENCES

[1]. Jeong P, Moon Y, Lee JH, et al. Discovery of orally active indirubin-3'-oxime derivatives as potent type 1 FLT3 inhibitors for acute myeloid leukemia. Eur J Med Chem. 2020;195:112205.



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