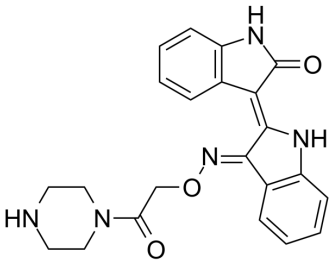
FLT3/D835Y-IN-1

Cat. No.:	HY-143434
CAS No.:	2648799-49-7
Molecular Formula:	$C_{22}H_{21}N_5O_3$
Molecular Weight:	403.43
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/D835Y-IN-1 (compound 13a) is a orally active, potent and selective FLT3 and FLT3/D835Y inhibitor, with IC_{50} values of 0.26 nM and 0.18 nM, respectively. FLT3/D835Y-IN-1 also blocks tumor growth, has anticancer efficacy, and can be used to research for AML (acute myeloid leukemia)[1].

IC_{50} & Target

FLT3/D835Y
0.18 nM (IC_{50})

In Vitro

FLT3/D835Y-IN-1 (compound 13a) (100 nM, 3 h) potently inhibits Ba/F3-FLT3-ITD, Ba/F3-FLT3-ITD/D835Y, Ba/F3-FLT3-ITD-F691L cell lines, and AML cells proliferation[1].
FLT3/D835Y-IN-1 (3-30 nM, 16 h) significantly inhibit FLT3, AKT, ERK, and STAT5 pathways[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay

Cell Line:	Ba/F3-FLT3-ITD, Ba/F3-FLT3-ITD/D835Y, and Ba/F3-FLT3-ITD-F691L cell lines, AML cells[1]
Concentration:	100 nM
Incubation Time:	3 h
Result:	Inhibited Ba/F3-FLT3-ITD, Ba/F3-FLT3-ITD/D835Y, Ba/F3-FLT3-ITD-F691L, MV4-11, MOLM14, and MOLM14-ITD/D835Y proliferation, with GI_{50} values of 0.59, 0.73, 5.54, 1.30, 6.20, and 4.58 nM, respectively.

Western Blot Analysis

Cell Line:	MOLM14-ITD/D835Y and MOLM14-ITD/F691L cells[1].
Concentration:	3, 10, and 30 nM
Incubation Time:	16 h
Result:	Significantly inhibited the FLT3, AKT, ERK, and STAT5 pathways at lower dosages.

In Vivo

FLT3/D835Y-IN-1 (10 mg/kg, IP, daily, 6 days per week) significantly suppresses tumor growth and exhibits potent antitumor activity against MOLM14-ITD/D835Y cells[1].

FLT3/D835Y-IN-1 (10 mg/kg, IV or Orally, single) displays extremely low AUC and high clearance[1].
Pharmacokinetic Parameters of FLT3/D835Y-IN-1 in ICR mice[1].

Parameters	13a
AUC_{last} (ng*h/mL)	1360 ± 110
CL (L/h/kg)	6.96 ± 0.66
V_{ss} (L/kg)	14.8 ± 0.7
$T_{1/2}$ (h)	1.5 ± 0.1

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

Animal Model:	NOD/SCID mice (6 weeks, male, nine mice per group)[1]
Dosage:	10 mg/kg
Administration:	IP, daily, 6 days per week, from day 7 to day 29
Result:	Significantly suppressed tumor growth.

Animal Model:	ICR mice (7–8 weeks, male)[1]
Dosage:	10 mg/kg, dissolved in a solution (10% DMSO, 40% PEG400, and 50% PBS)
Administration:	IV or Orally, single (Pharmacokinetic Analysis)
Result:	Displayed extremely low AUC and high clearance.

REFERENCES

[1]. Lee JH, Shin JE, Kim W, et al. Discovery of indirubin-3'-aminooxy-acetamide derivatives as potent and selective FLT3/D835Y mutant kinase inhibitors for acute myeloid leukemia. Eur J Med Chem. 2022 Apr 21;237:114356.

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