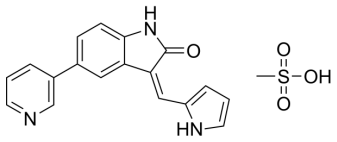
JI6

Cat. No.:	HY-18949
CAS No.:	856436-16-3
Molecular Formula:	$C_{19}H_{17}N_3O_4S$
Molecular Weight:	383.42
Target:	FLT3; JAK; c-Kit
Pathway:	Protein Tyrosine Kinase/RTK; Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

JI6 is a potent, selective and orally active FLT3 inhibitor, with IC_{50}s of -40, 8, and 4 nM for FLT3-WT, FLT3-D835Y, and FLT3-D835H, respectively. JI6 also inhibits JAK3 and c-Kit, with IC_{50}s of -250 and -500 nM, respectively. JI6 can be used for the research of acute myeloid leukemia[1].

IC_{50} & Target

FLT3-D835H 4 nM (IC_{50})	FLT3-D835Y 8 nM (IC_{50})	FLT3-WT 40 nM (IC_{50})	JAK3 ~250 nM (IC_{50})
c-Kit ~500 nM (IC_{50})			

In Vitro

JI6 (3-1000 nM; 1-4 days) selectively inhibits the viability of MV4-11 cells in a dose-dependent manner, with an IC_{50} of ~25 nM [1].

JI6 (1-2000 nM; 48 h) potently inhibits the viability of HCD-57 cells expressing FLT3-ITD, FLT3-D835Y, and FLT3-D835H with IC $_{50}$s of ~40 nM, but it displays essentially no effects on the parent HCD-57 or the cells transformed with JAK2V617F[1].

JI6 (100-500 nM; 24 h) induces apoptosis and cell cycle arrest in both FLT3-ITD- and FLT3-D835Y-expressing HCD-57 cells[1].

JI6 (50-500 nM; 3 h) inhibits phosphorylation of FLT3 and its downstream signaling transducers including ERK and Akt in FLT3-ITD- and FLT3-D835Y-transfromed HCD-57 cells[1].

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

Cell Viability Assay[1]

Cell Line:	MV4-11, HL60, Karpas 299, and Jurkat cells
Concentration:	3-1000 nM
Incubation Time:	48 hours
Result:	Inhibited MV4-11 cells and no effects of JI6 on the three remaining cells at a concentration as high as 1 μM.

Apoptosis Analysis[1]

Cell Line:	FLT3-ITD- and FLT3-D835Y-transformed HCD-57 cells
Concentration:	100, 500 nM

Incubation Time:	24 hours
Result:	Increased the percentage of apoptotic and necrotic cells and displayed no effects on the apoptosis of the parent HCD-57 cells.

Cell Cycle Analysis[1]

Cell Line:	FLT3-ITD- and FLT3-D835Y-transformed HCD-57 cells
Concentration:	100, 500 nM
Incubation Time:	24 hours
Result:	Significantly reduced G2 and S phase cells and increased G1 phase cells in both FLT3-ITD and D835Y cells.

Cell Viability Assay[1]

Cell Line:	FLT3-ITD- and FLT3-D835Y-transformed HCD-57 cells
Concentration:	50, 100, 500 nM
Incubation Time:	3 hours
Result:	Inhibited phosphorylation of FLT3, ERK1, ERK2 and Akt.

In Vivo

JI6 (15 mg/kg; i.p. daily for 3 weeks) inhibits the proliferation of FLT3-D835Y-transformed HCD-57 in immunodeficient mice and prolongs the mice survival[1].
JI6 (25 mg/kg; p.o. daily for 3 weeks) suppresses myeloproliferative phenotypes in FLT3-ITD knock-in mice[1].
JI6 (100 mg/kg; a single i.p.) significantly inhibits phosphorylation of FLT3 and downstream signal transductionin mice expressing FLT3-D835Y[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	NSG mice (10-12 weeks old, male) were implanted with FLT3-D835Y-transformed HCD-57 cells[1]
Dosage:	15 mg/kg
Administration:	I.p. daily for 3 weeks
Result:	Reduced the spleen size and prolonged the survival of these mice.

REFERENCES

[1]. Chen Y, et, al. Identification of an orally available compound with potent and broad FLT3 inhibition activity. Oncogene. 2016 Jun 9;35(23):2971-8.

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