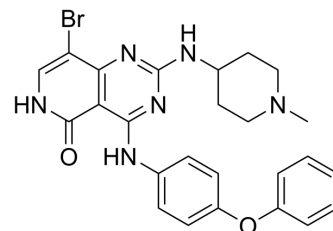


Denfivontinib

Cat. No.:	HY-12333
CAS No.:	1457983-28-6
Molecular Formula:	C ₂₅ H ₂₅ BrN ₆ O ₂
Molecular Weight:	521.41
Target:	FLT3; Apoptosis
Pathway:	Protein Tyrosine Kinase/RTK; Apoptosis
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro	DMSO : 25 mg/mL (47.95 mM; Need ultrasonic)					
	Preparing Stock Solutions	<div><div>Solvent</div><div>Concentration</div></div>	Mass	1 mg	5 mg	10 mg
		1 mM		1.9179 mL	9.5894 mL	19.1788 mL
		5 mM		0.3836 mL	1.9179 mL	3.8358 mL
		10 mM		0.1918 mL	0.9589 mL	1.9179 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: ≥ 2.5 mg/mL (4.79 mM); Clear solution					
	2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (4.79 mM); Suspended solution; Need ultrasonic					
	3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: ≥ 2.5 mg/mL (4.79 mM); Clear solution					

BIOLOGICAL ACTIVITY

Description	Denfivontinib (G-749) is a potent, oral active and ATP competitive FLT3 inhibitor, with IC ₅₀ s of 0.4 nM and 0.6 nM for FLT3 wild type and FLT3-D835Y, respectively. Denfivontinib can be used for the research of agent resistance for acute myeloid leukemia (AML) ^[1] .
IC ₅₀ & Target	IC ₅₀ : 0.4 nM (FLT3-WT), 0.6 nM (FLT3-D835Y) ^[1]
In Vitro	Denfivontinib shows potent and sustained inhibition of the FLT3 wild type and mutants including FLT3-ITD, FLT3-D835Y,

FLT3-ITD/N676D, and FLT3-ITD/F691L in cellular assays^[1].

Denfivontinib inhibits autophosphorylation of FLT3 with an IC₅₀ value of ≤8 nM in FLT3-WT bearing RS4-11 and in FLT3-ITD harboring MV4-11 and Molm-14 cells^[1].

Denfivontinib (0.0001-10 nM; 72 hours) shows strong antiproliferation of leukemia cells addicted to FLT3-ITD (MV4-11 and Molm-14) in a dose-dependent manner^[1].

Denfivontinib (25-100 nM; 36 hours) causes antiproliferative activity through apoptosis^[1].

Denfivontinib (1.6-1000 nM; 2 hours) shows more potent inhibition of p-FLT3, p-ERK1/2, and p-AKT than AC220 and PKC412^[1].

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

Cell Proliferation Assay^[1]

Cell Line:	MV4-11 cells, Molm-14 cells, K562 cells, HEL cells, RS4-11 cells
Concentration:	0.0001-10 nM
Incubation Time:	72 hours
Result:	Had antiproliferative activity for leukemia cells addicted to FLT3-ITD.

Apoptosis Analysis^[1]

Cell Line:	MV4-11 cells
Concentration:	25 nM, 50 nM, 100 nM
Incubation Time:	36 hours
Result:	Increased apoptosis of MV4-11 cells in a dose-dependent manner.

Western Blot Analysis^[1]

Cell Line:	Molm-14 cells
Concentration:	1.6 nM, 80 nM, 40 nM, 200 nM, 1000 nM
Incubation Time:	2 hours
Result:	Inhibited the phosphorylation of downstream effectors in the FLT3 signaling pathway, such as p-STAT5, p-AKT, p-ERK1/2, and p-FoxO3a.

In Vivo

Denfivontinib (3-30 mg/kg; p.o.; daily; for 28 days) shows effective antitumor activity in mouse models^[1].

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

Animal Model:	Athymic nu/nu mice, subcutaneous MV4-11 xenograft mice ^[1]
Dosage:	3 mg/kg, 10 mg/kg, 30 mg/kg
Administration:	Oral administration, daily, for 28 days
Result:	Suppressed tumor growth.

REFERENCES

[1]. Lee HK, et al. G-749, a novel FLT3 kinase inhibitor, can overcome drug resistance for the treatment of acute myeloid leukemia. Blood. 2014 Apr 3;123(14):2209-19.

Caution: Product has not been fully validated for medical applications. For research use only.

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