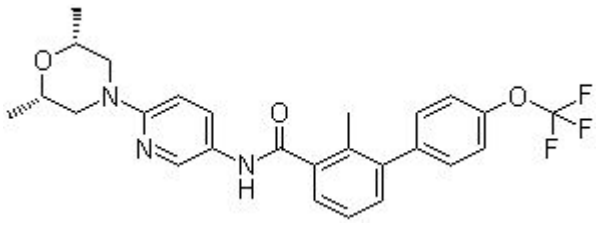
Product Introduction

LDE225 (NVP-LDE225,Erismodegib)

LDE225 (NVP-LDE225) is a **Smoothened** (Smo) antagonist, inhibiting **Hedgehog** (Hh) signaling with **IC50** of 1.3 nM (mouse) and 2.5 nM (human), respectively. Phase 3.

Technical Data:

Molecular Weight (MW):	485.5	
Formula:	$C_{26}H_{26}F_3N_3O_3$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 97 mg/mL	
	Water <1 mg/mL	
	Ethanol 97 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	956697-53-3	

Biological Activity

LDE225 inhibits TM3 luciferized cell line with 0.6 nM and 8 nM, at the presence of 1 nM and 25 nM Hh agonist Ag1.5, respectively. [1]

LDE225 is highly bound to mouse, rat, and human plasma proteins (>99%) and moderately bound to dog and monkey plasma proteins (77 and 85%, respectively). LDE225 has high permeability (90.8% in man) in the PAMPA assay. LDE225 shows good oral bioavailability ranging from 69 to 102% in preclinical species

when dosed in solution. LDE225 is a weak base with a measured pK_a of 4.20 and exhibits relatively poor aqueous solubility. LDE225 demonstrates dose-related antitumor activity. At a dose of 5 mg/kg/day qd, LDE225 significantly inhibits tumor growth, corresponding to a T/C value of 33%. When dosed at 10 and 20 mg/kg/day qd, LDE225 gives rise to 51 and 83% regression, respectively. Gli1 mRNA inhibition correlates with tumor and plasma exposure of LDE225. LDE225 successfully penetrates the blood–brain barrier in tumor-bearing animals and results in tumor growth inhibition after 4 days of treatment. [1] LDE225 significantly reduces the tumor volume by 95.7% in Rip1-Tag2 mice. LDE225 prolongs survival in Rip1Tag2 mice. LDE225 decreases expression of stromal markers in the LDE225-treated mice. [2]

References

[1] Pan SF, et al. ACS Med. Chem. Lett., 2010, 1 (3), 130–134.

[2] Fendrich V, et al. Ann Surg, 2011, 254(5), 818-23.

[3] Tauchi T, et al. Arthritis Res Ther, 2012, 14(Suppl 1), O43.

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