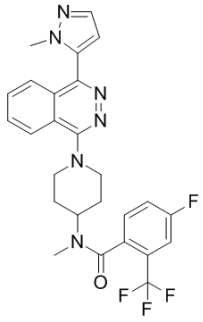
Taladegib

Cat. No.:	HY-13242
CAS No.:	1258861-20-9
Molecular Formula:	$C_{26}H_{24}F_4N_6O$
Molecular Weight:	512.5
Target:	Smo
Pathway:	Stem Cell/Wnt
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (97.56 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9512 mL	9.7561 mL	19.5122 mL
	5 mM	0.3902 mL	1.9512 mL	3.9024 mL
	10 mM	0.1951 mL	0.9756 mL	1.9512 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 (4.88 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.88 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.88 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Taladegib (LY2940680) is an antagonist of the smoothened receptor.

IC_{50} & Target

Smo[1]

In Vitro

Taladegib, a small-molecule antagonist of the smoothened receptor, shows a slight inhibitory effect on cell proliferation without differences between mucin- (IC_{50}: Taladegib=49.8±4.5 μM) and mixed- Cholangiocarcinoma (CCA) (IC_{50}: Taladegib=61.2±21.1 μM)[1]. The IC_{50} for Taladegib inhibition of [^{3}H]MRT-92 binding is right shifted (3- to 100-fold) for the

S387A^{ECL2}, L325F$^{3.36f}$, and D473H$^{6.54f}$ mutants but did not differ from that of WT receptor for the other mutants. The ability of SANT-1 to inhibit [^{3}H]MRT-92 binding to V329F$^{3.40f}$ and T466F$^{6.47f}$ mutants is abolished, and it is severely impaired for L325F$^{3.40f}$, I408F$^{5.51f}$, and M525G$^{7.45f}$ mutants (4- to 140-fold drop of the IC_{50}), but is not modified for the S387A^{ECL2} mutant. Taken together, these data confirm our docking hypothesis that MRT-92-binding mode differs from that of either Taladegib or SANT-1 by simultaneously occupying binding sites 1 and 2[2].

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

CUSTOMER VALIDATION

- J Genet Genomics. 2018 May 20;45(5):237-246.

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REFERENCES

[1]. Fraveto A, et al, Sensitivity of Human Intrahepatic Cholangiocarcinoma Subtypes to Chemotherapeutics and Molecular Targeted Agents: A Study on Primary Cell Cultures. PLoS One. 2015 Nov 16;10(11):e0142124.

[2]. Hoch L, et al. MRT-92 inhibits Hedgehog signaling by blocking overlapping binding sites in the transmembrane domain of the Smoothened receptor. FASEB J. 2015 May;29(5):1817-29.

[3]. Ma W, et al. Reduced Smoothened level rescued Aβ-induced memory deficits and neuronal inflammation in animal models of Alzheimer's disease. J Genet Genomics. 2018 May 20;45(5):237-246.

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