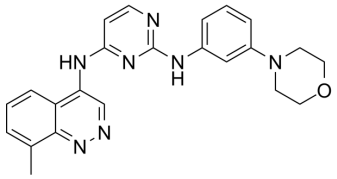
ALK5-IN-34

Cat. No.:	HY-151289
CAS No.:	2785430-90-0
Molecular Formula:	$C_{23}H_{23}N_7O$
Molecular Weight:	413.48
Target:	TGF-β Receptor; TGF-beta/Smad
Pathway:	TGF-beta/Smad; 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 : 100 mg/mL (241.85 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4185 mL	12.0925 mL	24.1850 mL
	5 mM	0.4837 mL	2.4185 mL	4.8370 mL
	10 mM	0.2418 mL	1.2092 mL	2.4185 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 (6.05 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (6.05 mM); Clear solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (6.05 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

ALK5-IN-34 is an selective orally active activin receptor-like kinase (ALK) inhibitor. ALK5-IN-34 can inhibit the activity of ALK5-IN-34 with an IC_{50} value of ≤10 nM. ALK5-IN-34 also has inhibitory of tumor growth and can be used for the research of proliferative diseases, such as cancer[1].

IC_{50} & Target

ALK5
<10 nM (IC_{50})

In Vitro

ALK5-IN-34 (EX-11) has kinase inhibition of ALK5 with an IC_{50} value of ≤10 nM[1].
ALK5-IN-34 has kinase selectivity of ALK2/ALK5 with an IC_{50} value of ⊠100 nM[1].
ALK5-IN-34 shows TGFB-RI inhibition (RD-SMAD receptor activity) with an IC_{50} value of ≤100 nM[1].
ALK5-IN-34 (1 μM-10 nM) inhibits the expression of TGF-β-mediated alpha-SMA in a full concentration-dependent[1].
ALK5-IN-34 (30, 300 and 3000 nM) suppresses the Treg frequency in a dose dependent manner[1].
ALK5-IN-34 (0-0.1 μM; for 6 days or 7 days) inhibits $FOXL2^{Cl34W}$-driven growth in KGN and COV434 cells with IC50 values of 140 nM and >10 μM, respectively[1].
ALK5-IN-34 (10, 100 and 1000 nM; 2 h) shows a dose-dependent decrease in pSmad2 in KGN cell line[1].
ALK5-IN-34 (30, 300 nM; 24 h) reverses the upregulation of gene expression in dose dependentent[1].
ALK5-IN-34 (30, 300 nM; 24 h) increases HLA class I expression in dose-dependent[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	KGN and COV434 cell lines
Concentration:	0-0.1 μM
Incubation Time:	for 6 days or 7 days
Result:	Inhibited $FOXL2^{Cl34W}$-driven growth.

RT-PCR[1]

Cell Line:	Human primary dermal fibroblasts
Concentration:	30, 300 nM
Incubation Time:	24 h
Result:	Reversed the upregulation of gene expression with TGFB stimulation.

In Vivo

ALK5-IN-34 (EX-11) (oral; 10-100 mg/kg) reduces the phopho SMAD2 levels (p-SMAD2) in a dose dependent manner in A549 murine xenograft model[1].
ALK5-IN-34 (oral; 75 mg/kg; 0-24 h) shows reversely correlated between PK and tumor PD (pSMAD2 levels)[1].
ALK5-IN-34 (oral; 150 mg/kg; bid; for 22 days) increases overall survival in ES-2 ovarian cancer mouse xenograft model and can delay progression[1].
ALK5-IN-34 (p.o.; 75, 150 mg/kg; twice a day; for 21days) shows tumor growth inhibition (TGI) and increases the survival when combining with anti-PD-L1/anti-PD-1 in Syngeneic TNBC Model and in Subcutaneous Cloudman S91 melanoma model [1].
ALK5-IN-34 (oral; 300, 1000 mg/kg; bid for 5 days) has good tolerability and safety margin in Tolerability Model[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	A549 murine xenograft model[1]
Dosage:	10, 50, 75 and 100 mg/kg
Administration:	oral gavage
Result:	Exhibited 92.5% inhibition based upon the average p-SMAD2 levels (75 mg/kg).

Animal Model:	EMT6 Syngeneic TNBC Model[1]
Dosage:	75, 150 mg/kg
Administration:	p.o., twice a day, for 21days

Result:	Resulted significantly tumor growth inhibition (TGI) by 37% at 150 mg/kg. Result in significant tumor growth inhibition (TGI) with combination of anti-PD-LI and resulted in a significant increase in mean survival by 37%. Resulted in significant TGI by 34% with combination of anti-PD-1 and resulted in significant increase in mean survival by 26%. Decreased the intra-tumoral pressure.

Animal Model:	Cachexia Model[1]
Dosage:	150 mg/kg
Administration:	oral gavage, twice a day for 22 days
Result:	Showed reduction in total fluid volume and high whole limb weights.

REFERENCES

[1]. Bettina FRANZ, et al. Alk-5 inhibitors and uses thereof. Patent. WO2022126133A1.

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