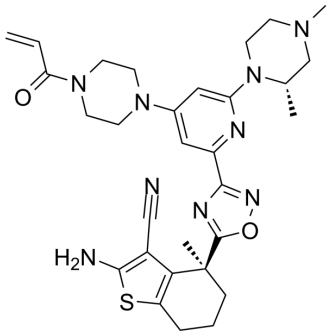
BI-0474

Cat. No.:	HY-148278
CAS No.:	2750570-55-7
Molecular Formula:	$C_{30}H_{37}N_9O_2S$
Molecular Weight:	587.74
Target:	Ras
Pathway:	GPCR/G Protein; MAPK/ERK Pathway
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 (170.14 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7014 mL	8.5072 mL	17.0143 mL
	5 mM	0.3403 mL	1.7014 mL	3.4029 mL
	10 mM	0.1701 mL	0.8507 mL	1.7014 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 (4.25 mM); Clear solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: 2.5 mg/mL (4.25 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

BI-0474 is a potent $KRAS^{G12C}$ inhibitor with an IC_{50} value of 7.0 nM for the GDP-KRAS::SOS1 protein-protein interaction. BI-0474 exhibits good anti-proliferative activity against NCI-H358 cells carrying the G12C mutation. BI-0474 also shows good anti-tumour activity in non-small cell lung cancer xenograft models[1].

IC_{50} & Target

KRAS-SOS1
7.0 nM (IC_{50})

In Vitro

BI-0474 (1-10,000 nM; 3 days) shows potent antiproliferative activity of 26 nM on NCI-H358 cells carrying a G12C mutation[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Proliferation Assay[1]

Cell Line:	NCI-H358 cells (carrying a G12C mutation)
Concentration:	1-10,000 nM
Incubation Time:	3 days
Result:	Inhibited proliferation of NCI-H358 cells with an EC_{50} of 26 nM.

In Vivo

BI-0474 (40 mg/kg; i.p.; single daily for 3 days) shows anti-tumor efficacy and pharmacodynamic biomarker modulation in an NCI-H358 cell line-derived non-small cell lung cancer xenograft model[1].

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

Animal Model:	NMRI nude mice (NCI-H358 cell line-derived non-small cell lung cancer xenograft model)[1] .
Dosage:	40 mg/kg
Administration:	Intraperitoneal administration; single daily for 3 days
Result:	Led to induction of programmed cell death in this xenograft model.

REFERENCES

[1]. Bröker J, et al. Fragment Optimization of Reversible Binding to the Switch II Pocket on KRAS Leads to a Potent, In Vivo Active KRASG12C Inhibitor. J Med Chem. 2022 Oct 27.

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