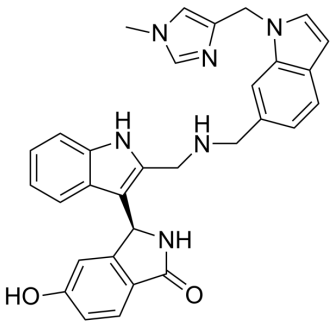
BI-2852

Cat. No.:	HY-126247
CAS No.:	2375482-51-0
Molecular Formula:	$C_{31}H_{28}N_6O_2$
Molecular Weight:	516.59
Target:	Ras
Pathway:	GPCR/G Protein
Storage:	4°C, stored under nitrogen * In solvent : -80°C, 2 years; -20°C, 1 year (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 55 mg/mL (106.47 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9358 mL	9.6789 mL	19.3577 mL
5 mM	0.3872 mL	1.9358 mL	3.8715 mL
10 mM	0.1936 mL	0.9679 mL	1.9358 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 (4.84 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.84 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.84 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BI-2852 is a KRAS inhibitor for the switch I/II pocket (SI/II-pocket) by structure-based agent design with nanomolar affinity. BI-2852 is mechanistically distinct from covalent KRASG12C inhibitor (binds to switch II pocket) and binds ten-fold more strongly to active KRASG12D versus KRASwt (740 nM vs 7.5 μM). BI-2852 blocks GEF, GAP, and effector interactions with KRAS, leading to inhibition of downstream signaling and an antiproliferative effect in KRAS mutant cells.

IC_{50} & Target		
	KRAS(G12C) 450 nM (IC_{50})	KRAS(G12C) 750 nM (Kd)

In Vitro

BI-2852 (Compound 1) (10 nM-10 μM; 2 hours) shows a dose-dependent pERK modulation and antiproliferative effect at EC_{50}

s of 5.8 μM and 6.7 μM in soft agar and low serum conditions in NCI-H358 cells[1].

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

REFERENCES

[1]. Kessler D, et al. Drugging an undruggable pocket on KRAS. Proc Natl Acad Sci U S A. 2019 Aug 6; 116(32):15823-15829.

[2]. Dirk Kessler, et al. Drugging all RAS isoforms with one pocket. FUTURE MEDICINAL CHEMISTRY

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