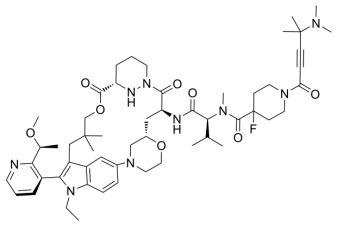
RMC-6291

Cat. No.:	HY-153346
CAS No.:	2641998-63-0
Molecular Formula:	$C_{55}H_{78}FN_9O_8$
Molecular Weight:	1012.26
Target:	Ras; ERK; Apoptosis
Pathway:	GPCR/G Protein; MAPK/ERK Pathway; Stem Cell/Wnt; Apoptosis
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (98.79 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	0.9879 mL	4.9394 mL	9.8789 mL
	5 mM	0.1976 mL	0.9879 mL	1.9758 mL
	10 mM	0.0988 mL	0.4939 mL	0.9879 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 (2.47 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (2.47 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (2.47 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

RMC-6291 is an orally active and covalent inhibitor of $KRAS^{G12C}$(ON). RMC-6291 forms a tri-complex within tumor cells between $KRAS^{G12C}$(ON) and cyclophilin A (CypA). Thus, RMC-6291 prevents $KRAS^{G12C}$(ON) from signaling via steric blockade of RAS effector binding. RMC-6291 inhibits ERK signaling and induced apoptosis in KRASG12C-mutant H358 cells. RMC-6291 also inhibits the proliferation of $KRAS^{G12C}$ mutant cells with a median IC_{50} of 0.11 nM[1][2].

IC_{50} & Target

KRAS(G12C)

In Vivo

RMC-6291 (200mg/kg, p.o., qd for 60 d) significantly inhibits tumor growth and induce immunological memory in murine

tumor models[3].

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

REFERENCES

[1]. Nichols R J, et al. RMC-6291, a next-generation tri-complex KRASG12C (ON) inhibitor, outperforms KRASG12C (OFF) inhibitors in preclinical models of KRASG12C cancers[J]. Cancer Research, 2022, 82(12_Supplement): 3595-3595.

[2]. Cristina Blaj, et al. Enhancement of anti-tumor immunity in immunogenic and immune-refractory RAS mutant tumors with tri-complex RAS(ON) inhibitors, revmed, #PB044, 2022

[3]. Schulze CJ, et al. Chemical remodeling of a cellular chaperone to target the active state of mutant KRAS. Science. 2023 Aug 18;381(6659):794-799.

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