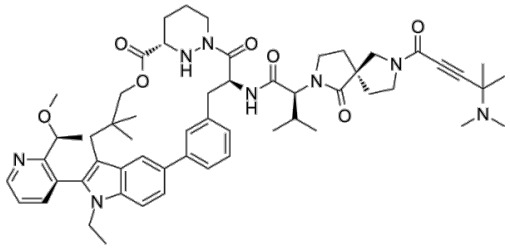
Product Data Sheet

Product Name: RMC-4998
Cat. No.: GC73678

Chemical Properties

Cas. No.	2642037-07-6		
Formula	$C_{57}H_{74}N_8O_7$	M.Wt	983.25
Solubility		Storage	4°C, stored under nitrogen
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			



Background

RMC-4998 is an orally active inhibitor targeting the active or GTP-bound state of the KRASG12C mutant. RMC-4998 can form a ternary complex with intracellular CYPA and the activated KRASG12C mutant, with an IC50 value of 28 nM. RMC-4998 can inhibit ERK signaling in KRASG12C mutant cancer cells and induce apoptosis. RMC-4998 can be used for tumor research.

RMC-4998 (100 nM, 120 h) disrupts oncogenic signaling in KRASG12C mutant cells by recruiting cyclophilin A (CYPA) to the active state of mutant KRAS[1].RMC-4998 can inhibit the expression of ERK signaling related proteins and cell proliferation in KRASG12C mutant cancer cells[1].RMC-4998

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(0-1000 nM, 72 h) inhibits lung cancer cell viability by suppressing the PI3K/mTOR and ERK signaling pathways[2].RMC-4998 (30 nM, 96 h) can inhibit ERK protein phosphorylation and suppress LU65 cell viability[3].

RMC-4998 (10-200 mg/kg; once daily; 28 days; p.o.) inhibits ERK phosphorylation in tumors and exhibits anti-tumor activity in mice carrying NCI-H358 xenografts[1].RMC-4998 (80 mg/kg; once daily; 4 weeks; p.o.) can promote tumor regression in non-small cell lung cancer mice and has anti-tumor activity[2].RMC-4998 (100 mg/kg; once daily; p.o.) induces tumor regression and inhibits ERK phosphorylation expression in sotorasib-R LU65 xenograft mice[3].

References:
[1]. 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.
[2]. Kitai H,et al. Combined inhibition of KRASG12C and mTORC1 kinase is synergistic in non-small cell lung cancer. Nat Commun. 2024 Jul 19;15(1):6076.
[3]. Solanki H S, et al. RTK signaling and WT RAS activity as vulnerabilities in tumors with acquired resistance to GDP-state selective KRASG12C inhibitors in preclinical models[J]. Cancer Research, 2024, 84(6_Supplement): 1924-1924.

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