Product Data Sheet

Product Name: RMC-9945
Cat. No.: GC79246

Chemical Properties

Cas. No.	2922732-38-3		
Formula	$C_{60}H_{80}F_3N_{11}O_6S$	M.Wt	1140.41
Solubility	DMSO: 100 mg/mL (87.69 mM; Need ultrasonic)	Storage	Store at -20°C
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-9945 (RM-044) is a selective, covalent, and orally active RAS (ON) G12D inhibitor. RMC-9945 enhances the transcriptional activity of β-Catenin/TCF. RMC-9945 induces cell state transition, forcing metastatic colorectal cancer cells to switch from the Emp1 + state to the Lgr5 + stem cell-like state. RMC-9945 achieves durable disease control in preclinical models of colorectal cancer with early liver metastasis, but shows reduced activity in late-stage metastasis models. RMC-9945 can be

used in research related to metastatic colorectal cancer and pancreatic ductal adenocarcinoma [1] [2] [3].

In Vivo, RMC-9945 (100 mg/kg; p.o.; daily) achieves durable disease control in an early-stage liver metastatic colorectal cancer model, but its therapeutic benefit diminishes in advanced disease due to the conversion of Emp1+ HRC into drug-resistant Lgr5+ CSC; combination treatment with RMC-9945 (100 mg/kg; p.o.; daily) and Lgr5+ CSC ablation (DT 25 μg/kg; i.p.) yields significant responses and prolongs survival[1]. RMC-9945 (100 mg/kg; p.o.; once daily; for 28 consecutive days) inhibits preneoplastic lesion burden in KPC mice, delays PDAC tumorigenesis, extends median overall survival by approximately 80 days, and does not select for more aggressive tumors[3]. RMC-9945 (100 mg/kg; p.o.; once daily; for 10 consecutive days) significantly reduces pancreatic tumor burden in KPC mice by inducing apoptosis of tumor epithelial cells while inhibiting the RAS signaling pathway[3].

In Vitro, RMC-9945 (100 nM) transiently inhibits the growth of AKTP MTO in vitro, induces the transition from the Emp1+ HRC state to the Lgr5+ CSC state, and enhances the transcriptional activity of β-catenin/TCF by upregulating TCF/LEF transcription factors[1]. RMC-9945 (100 nM; 4-10 days) induces the transition from the EMP1+ HRC state to the LGR5+ CSC state in KRASG12D-mutated colorectal cancer organoids, and its growth inhibitory activity varies across different models[1]. RMC-9945 (100 nM) alters chromatin accessibility in AKTP MTO, reduces the regulatory effect of AP1 on HRC-related genes, and enhances the regulatory effect of LEF/TCF on Lgr5+ CSC-related genes, without inducing large-scale changes in chromatin topology[1].

References:
[1]. Centonze A, et al. A Plastic EMP1+ to LGR5+ Cell State Conversion as a Bypass to KRASG12D Pharmacologic Inhibition in Metastatic Colorectal Cancer. Cancer discovery. 2026 Feb 06;16(2):320-344.
[2]. Bu J, et al. Cancer Stem Cells in Human Gastrointestinal and Hepatic Cancers. MedComm (2020). 2025 Dec 3;6(12):e70513. doi: 10.1002/mco2.70513.
[3]. Vincent A, et al. Pancreatic cancer. Lancet (London, England). 2011 Aug 13;378(9791):607-20.