

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

Caution: Product has not been fully validated for medical applications. For research use only.

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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.

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