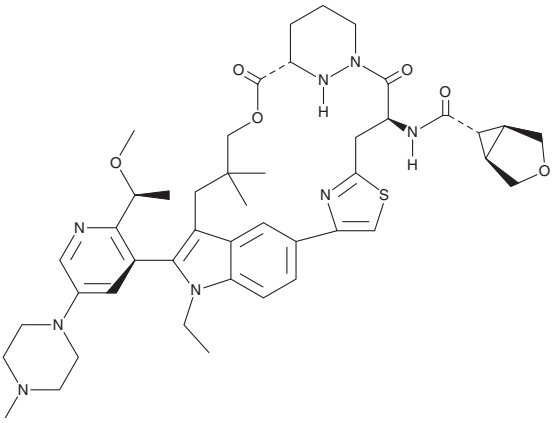
PRODUCT INFORMATION

RMC-7977

Item No. 42185

CAS Registry No.: 2765082-12-8
Formal Name: (1α,5α,6α)-N-[(2R,14S,18S)-2-[5-(4-cyclopropyl-1-piperazinyl)-2-[(1S)-1-methoxyethyl]-3-pyridinyl]-1-ethyl-18,19,20,21-tetrahydro-25,25-dimethyl-15,22-dioxo-17H-5,3-([4,2]-endo-thiazolopropano[1,3]-*endo*-pyridazinomethanoxypropano)-1H-indol-14-yl]-3-oxabicyclo[3.1.0]hexane-6-carboxamide
MF: $C_{47}H_{60}N_8O_6S$
FW: 865.1
Purity: ≥95%
Supplied as: A solid
Storage: -20°C
Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

RMC-7977 is supplied as a solid. A stock solution may be made by dissolving the RMC-7977 in the solvent of choice, which should be purged with an inert gas. RMC-7977 is soluble (≥10 mg/ml) in ethanol and DMSO.

Description

RMC-7977 is an inhibitor of wild-type and mutant Ras protein-protein interactions.[1] It inhibits the interaction between wild-type K-Ras and seven activating mutation-containing K-Ras variants and C-RAF (EC_{50}s = 5.06-34.5 nM) and the same K-Ras variants and cyclophilin A (EC_{50}s = 1.27-9.12 nM) in bioluminescence resonance energy transfer (BRET) assays using U2OS cells expressing the human proteins. RMC-7977 also inhibits the protein-protein interactions between wild-type N-Ras, N-Ras^{Q61K}, N-Ras^{Q61L}, and N-Ras^{Q61R} and B-RAF (EC_{50}s = 57.7, 53.9, 145, and 181 nM, respectively, in time-resolved FRET (TR-FRET) assays) and wild-type H-Ras and H-Ras^{G13R} and B-RAF (EC_{50}s = 59.9 and 23.7 nM, respectively, in TR-FRET assays). It has antiproliferative activity against a panel of 183 K-Ras-dependent cancer cell lines (median EC_{50} = 2.4 nM). RMC-7977 (10 nM) also reduces the proliferation of adagrasib-resistant NCI H358 non-small cell lung cancer (NSCLC) cells. It reduces tumor volumes in SW620 colon, HPAC pancreatic, and NCI H441 lung cancer mouse xenograft models when administered at a dose of 10 mg/kg per day.

Reference

1. Holderfield, M., Lee, B.J., Jiang, J., *et al*. Concurrent inhibition of oncogenic and wild-type RAS-GTP for cancer therapy. *Nature* **629(8013)**, 919-926 (2024).

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