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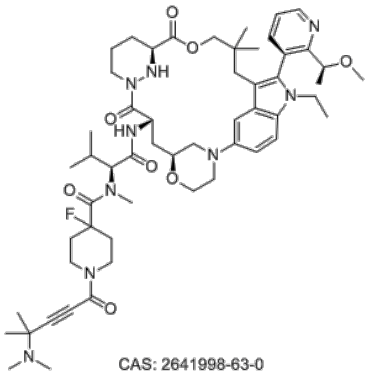
Data Sheet

Global Supplier of Chemical Probes, Inhibitors & Agonists.

Product Name	:	RMC-6291
Cat. No.	:	PC-20608
CAS No.	:	2641998-63-0
Molecular Formula	:	$C_{55}H_{78}FN_9O_8$
Molecular Weight	:	1012.28
Target	:	Ras
Solubility	:	10 mM in DMSO



Biological Activity

RMC-6291 (RMC6291) is a potent, covalent, next-generation, mutant-selective inhibitor of active state **KRAS G12C(ON)** with IC50 of 0.7 nM (pERK), RMC-6291 forms a tri-complex within tumor cells between KRASG12C(ON) and cyclophilin A (CypA).
RMC-6291 potently inhibits HCI-H358 cell growth (KRAS G12C) with IC50 of 0.09 nM, >10000-fold selectivity over WT cell.
RMC-6291 overcomes the limitations of first-generation KRASG12C(OFF) inhibitors in preclinical models by directly targeting the active form of KRAS G12C.
Oral administration of RMC-6291 produces deep and durable suppression of RAS pathway activity in KRASG12C tumor models and drives profound tumor regressions in vivo at well-tolerated doses.
RMC-6291 outperforms MRTX849 (Adagrasib, Cat. PC-72227), a KRASG12C(OFF) inhibitor, in mouse clinical trial consisting of multiple patient- and cell line-derived xenograft models of KRASG12C NSCLC.
Combination treatment with RMC-6291 and SHP2 or SOS1 inhibitors was well tolerated in preclinical models and further increased anti-tumor activity.
RMC-6291 also combined well with immune checkpoint inhibitors, sensitizing KRASG12C-bearing cancer models to anti-tumor immunity.

References

Robert J. Nichols, et al. ***Cancer Res*** (2022) 82 (12_Supplement): 3595.

Caution: Product has not been fully validated for medical applications. Lab Use Only!

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