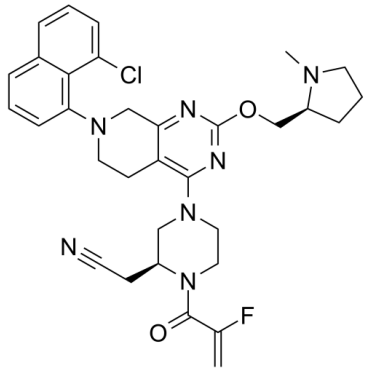
Data Sheet

Product Name:	Adagrasib
Cat. No.:	CS-0105265
CAS No.:	2326521-71-3
Molecular Formula:	$C_{32}H_{35}ClFN_7O_2$
Molecular Weight:	604.12
Target:	Ras
Pathway:	GPCR/G Protein
Solubility:	DMSO : 50 mg/mL (82.77 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Adagrasib (MRTX849) is a potent, orally-available, and mutation-selective covalent inhibitor of **KRAS G12C** with potential antineoplastic activity. Adagrasib covalently binds to KRAS G12C at the cysteine at residue 12, locks the protein in its inactive GDP-bound conformation, and inhibits KRAS-dependent signal transduction[1][2]. IC50 & Target:KRAS G12C[1] **In Vitro:** Adagrasib (MRTX849) (0.1-10000 nM; 3-day/2D conditions; 12-day/3D conditions) potently inhibits cell growth in the vast majority of KRAS G12C-mutant cell lines with IC_{50}s ranging between 10 and 973 nM in the 2D format and between 0.2 and 1042 nM in the 3D format[1]
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Adagrasib (0.24-1000 nM; 24 hours) inhibits KRAS-dependent signaling targets including ERK1/2 phosphorylation (Thr202/Tyr204 ERK1; pERK), S6 phosphorylation (RSK-dependent Ser235/236; pS6) and expression of the ERK-regulated DUSP6[1]. **In Vivo:** Adagrasib (1-100 mg/kg; i.g.; daily until day 16) demonstrates dose-dependent anti-tumor efficacy over a well-tolerated dose range, and the maximally efficacious dose of MRTX849 is between 30-100 mg/kg/day[1].

References:

[1]. Christensen JG, et al. The KRASG12C Inhibitor, MRTX849, Provides Insight Toward Therapeutic Susceptibility of KRAS Mutant Cancers in Mouse Models and Patients. Cancer Discov. 2019 Oct 28. pii: CD-19-1167.

[2]. Kyriakos P. Papadopoulos, et al. A phase I/II multiple expansion cohort trial of MRTX849 in patients with advanced solid tumors with KRAS G12C mutation. Journal of Clinical Oncology 2019 37:15_suppl, TPS3161-TPS3161.

[3]. Fell JB, Fischer JP, Baer BR, et al. Identification of the Clinical Development Candidate MRTX849, a Covalent KRASG12C Inhibitor for the Treatment of Cancer. J Med Chem. 2020;63(13):6679-6693.

[4]. Awad MM, Liu S, Rybkin II, et al. Acquired Resistance to KRASG12C Inhibition in Cancer. N Engl J Med. 2021;384(25):2382-2393.

CAIndexNames:

2-Piperazineacetonitrile, 4-[7-(8-chloro-1-naphthalenyl)-5,6,7,8-tetrahydro-2-[[(2S)-1-methyl-2-pyrrolidinyl]methoxy]pyrido[3,4-d]pyrimidin-4-yl]-1-(2-fluoro-1-oxo-2-propen-1-yl)-, (2S)-

SMILES:

N#CC[C@@H]1N(C(C(F)=C)=O)CCN(C2=C3C(CN(C4=C5C(Cl)=CC=CC5=CC=C4)CC3)=NC(OC[C@H]6N(C)CCC6)=N2)C1

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

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