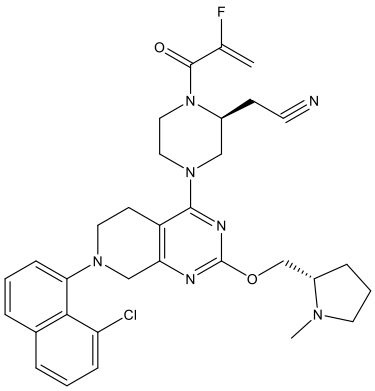
Catalog # 10-3928
MRTX849

CAS# 2326521-71-3

2-[(2S)-4-[7-(8-Chloronaphthalen-1-yl)-2-[[(2S)-1-methylpyrrolidin-2-yl]methoxy]-6,8-dihydro-5H-pyrido[3,4-d]pyrimidin-4-yl]-1-(2-fluoroprop-2-enoyl)piperazin-2-yl]acetonitrile; Adagrasib

Lot # FBS3069



MRTX849 is a potent (IC_{50}'s = 14 nM NCI-H358; 5 nM MIA PaCa-2) and selective (over 463 proteins @ 1 µM) covalent $KRAS^{G12C}$ inhibitor.[1] It showed pronounced tumor regression in 17 of 26 $KRAS^{G12C}$-positive cell lines and xenograft models from multiple tumor types.[2] MTRTX849 reversed the immunosuppressive tumor environment in a genetically modified mouse model and sensitized tumors to checkpoint inhibitor therapy in a genetically modified mouse $KRAS^{G12C}$ lung adenocarcinoma model.[3] It reversed ABCB1-mediated multidrug resistance *in vitro* and *in vivo* [via] attenuation of ABCB1 efflux in drug-resistant cancer cells.[4]

1) Fell *et al*. (2020), *Identification of the Clinical Development Candidate MRTX849, a Covalent $KRAS^{G12C}$ Inhibitor for the Treatment of Cancer*; J. Med. Chem. **63** 6679
2) Hallin *et al*. (2020); *The $KRAS^{G12C}$ Inhibitor, MRTX849, Provides Insight Toward Therapeutic Susceptibility of KRAS Mutant Cancers in Mouse Models and Patients*, Cancer Discov., **10** 54
3) Briere *et al*. (2021); *The $KRAS^{G12C}$ Inhibitor MRTX849 Reconditions the Tumor Immune Microenvironment and Sensitizes Tumors to Checkpoint Inhibitor Therapy*, Mol. Cancer Ther., **20** 975
4) Zhang *et al*. (2022); *Adagrasib, a KRAS G12C inhibitor, reverses the multidrug resistance mediated by ABCB1 in vitro and in vivo*, Cell Commun. Signal., **20** 142

PHYSICAL DATA

Molecular Weight:	604.13
Molecular Formula:	$C_{32}H_{35}ClFN_7O_2$
Purity:	>98% by HPLC
	NMR: (Conforms)
Solubility:	DMSO (>25 mg/ml)
Physical Description:	White solid
Storage and Stability:	Store as supplied at -20°C for up to 2 years from the date of purchase. Solutions in DMSO may be stored at -20°C for up to 1 month.

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