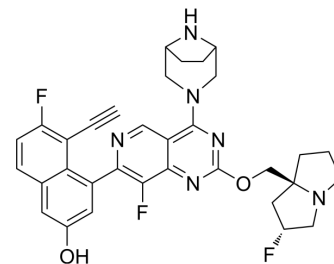


MRTX1133

Cat. No.:	HY-134813		
CAS No.:	2621928-55-8		
Molecular Formula:	C ₃₃ H ₃₁ F ₃ N ₆ O ₂		
Molecular Weight:	600.63		
Target:	Ras		
Pathway:	GPCR/G Protein		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (83.25 mM; Need ultrasonic)

Concentration	Solvent	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	1.6649 mL	8.3246 mL	16.6492 mL
	5 mM	0.3330 mL	1.6649 mL	3.3298 mL
	10 mM	0.1665 mL	0.8325 mL	1.6649 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% SBE-β-CD/50 mM citrate pH 5.0
Solubility: 10 mg/mL (16.65 mM); Clear solution; Need ultrasonic and warming and adjust pH to 5 with HCl and heat to 60°C
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: 3.5 mg/mL (5.83 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.5 mg/mL (4.16 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

MRTX1133 is a noncovalent, potent, and selective KRAS G12D inhibitor. MRTX1133 optimally fills the switch II pocket and extends three substituents to favorably interact with the protein, resulting in an estimated K_D against KRAS G12D of 0.2 pM. MRTX1133 prevents SOS1-catalyzed nucleotide exchange and/or formation of the KRAS G12D/GTP/RAF1 complex, thereby inhibiting mutant KRAS-dependent signal transduction. MRTX1133 selectively inhibits KRAS G12D mutant, but not KRAS wild-type, tumor cells. MRTX1133 has single digit nanomolar activity in cellular assays and marked in vivo efficacy in tumor models harboring KRAS G12D mutations^{[1][2]}.

IC₅₀ & Target	KRas G12D 0.2 pM (Kd)	
In Vitro	MRTX1133 inhibits ERK phosphorylation in the AGS cell line with an IC ₅₀ ranging 1-10 nM (AsPC-1, Panc 04.03, Panc 02.03, SW1990, GP2D, Suit2, A427, SNU1033, and HPAC cells). In a 2D viability assay, the IC ₅₀ of MRTX1133 is 6 nM against AGS cells (KRAS G12D), while demonstrating more than 500-fold selectivity against MKN1, a cell line which is dependent on KRAS for its growth and survival due to the amplification of wild-type KRAS ^[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.	
In Vivo	MRTX1133 displays efficacious in a KRAS G12D mutant xenograft mouse tumor model ^[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.	
	Animal Model:	6-8-weekold, female, athymic nude-Foxn1 ^{nu} mice (Panc 04.03 model) ^[1]
	Dosage:	3, 10, or 30 mg/kg
	Administration:	Intraperitoneal; twice a day for 28 days
	Result:	An antitumor efficacy study in this model resulted in MRTX1133 dose-dependent antitumor activity with 94% growth inhibition observed at 3 mg/kg BID (IP) and tumor regressions of -62% and -73% observed at 10 and 30 mg/kg BID (IP), respectively.

CUSTOMER VALIDATION

- Immunity. 2023 Nov 14;56(11):2570-2583.e6.
- bioRxiv. 2023 Oct 6.
- bioRxiv. 2023 Sep 17.

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REFERENCES

[1]. Wang X, et al. Identification of MRTX1133, a Noncovalent, Potent, and Selective KRAS G12D Inhibitor [published online ahead of print, 2021 Dec 10]. J Med Chem. 2021;10.1021/acs.jmedchem.1c01688.

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

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