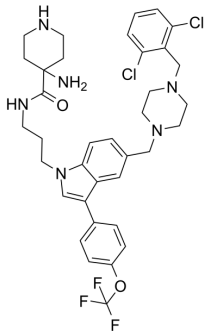
Pan-RAS-IN-1



Cat. No.:	HY-101295
CAS No.:	1835283-94-7
Molecular Formula:	$C_{36}H_{41}Cl_2F_3N_6O_2$
Molecular Weight:	717.65
Target:	Ras
Pathway:	GPCR/G Protein
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year

SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (69.67 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	1.3934 mL	6.9672 mL	13.9344 mL
	5 mM	0.2787 mL	1.3934 mL	2.7869 mL
	10 mM	0.1393 mL	0.6967 mL	1.3934 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (3.48 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (3.48 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.48 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Pan-RAS-IN-1 is a pan-Ras inhibitor that disrupts the interaction of Ras proteins and their effectors.

In Vitro

Pan-RAS-IN-1 binds to $KRas^{G12D}$-GppNHp with an affinity less than 20 μM. Pan-RAS-IN-1 binds to Ras proteins and exhibits lethality in cells partially dependent on expression of Ras proteins. The potency of pan-RAS-IN-1 correlates with the degree of dependency on the mutated isoform over a 5-fold concentration range. At some concentrations, pan-RAS-IN-1 is cytostatic, possibly due to pan-RAS inhibition. Pan-RAS-IN-1 is evaluated in primary T cell acute lymphoblastic leukemia (T-ALL) cells. Selective lethality is observed, with mutant NRAS cells retaining only 20%-40% viability after 5 μM treatment[1].

	MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Pan-RAS-IN-1 administration results in inhibition of tumor growth over 15 days of treatment. Pan-RAS-IN-1-treated mice exhibits decreased tumor pERK levels compared with vehicle treated mice. A modest increase in cleaved caspase-3 is also observed, showing that in this model, pan-RAS-IN-1 has the capacity to induce caspase activation[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	For 384-well cancer cell viability assays, cells are trypsinized, counted, and seeded into 384-well plates at 1,000 cells/well. After 16 hr, pan-RAS-IN-1 (from 10 mM stocks in DMSO) are arrayed in an 8-point or 16-point dilution series in 384-well polypropylene plates. Compound solutions are transferred at a 1:5 dilution into the assay plates. After 48 hr, a 50% Alamar blue solution is added to a final concentration of 10% Alamar blue. After 6 hr of incubation, fluorescence intensity is determined at 535 and 590 nm[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Mice tumor Xenograft are dosed with 180 mg/kg pan-RAS-IN-1 orally (12 mg/mL, 10% DMSO, pH 4), vehicle orally, or by a combination of i.p. and i.v. injections at 30 mg/kg (4 mg/mL, 5% DMSO in HBSS at pH 4). Over 14 d, mice receive a total of 10 doses of pan-RAS-IN-1 or vehicle orally, or six i.p. injections and 4 i.v. injections. Tumor size is measured by electronic caliper every 2 d and calculated[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Rep. 2021 Jul 6;36(1):109315.
- Cell Chem Biol. 2021 May 4;S2451-9456(21)00206-3.
- Antiviral Res. 2021 May 4;105082.
- Dis Model Mech. 2022 Feb 1;15(2):dmm049093.
- Neurooncol Adv. 31 December 2021.

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REFERENCES

[1]. Welsch ME, et al. Multivalent Small-Molecule Pan-RAS Inhibitors. Cell. 2017 Feb 23;168(5):878-889.e29.

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