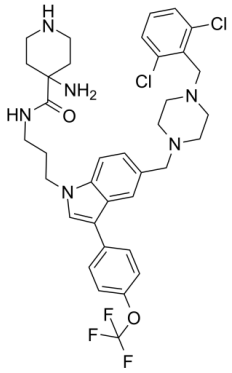
Data Sheet

Product Name:	Pan-RAS-IN-1
Cat. No.:	CS-6466
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
Solubility:	DMSO : ≥ 50 mg/mL (69.67 mM)



BIOLOGICAL ACTIVITY:

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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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]. **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].

References:

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

CAIndexNames:

4-Piperidinecarboxamide, 4-amino-N-[3-[5-[[4-[(2,6-dichlorophenyl)methyl]-1-piperazinyl]methyl]-3-[4-(trifluoromethoxy)phenyl]-1H-indol-1-yl]propyl]-

SMILES:

O=C(C1(N)CCNCC1)NCCCN2C3=CC=C(CN4CCN(CC5=C(Cl)C=CC=C5Cl)CC4)C=C3C(C6=CC=C(OC(F)(F)F)C=C6)=C2

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

Tel: 610-426-3128 Fax: 888-484-5008 E-mail: sales@ChemScene.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA