

Product Data Sheet

Product Name: Pan-RAS-IN-1

Cat. No.: GC32716

Chemical Properties

Cas. No. 1835283-94-7

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

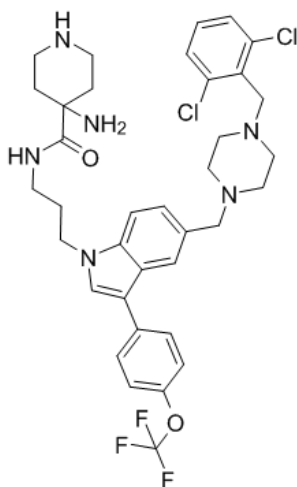
Formula $C_{36}H_{41}Cl_2F_3N_6O_2$ M.Wt 717.65

Solubility DMSO : ≥ 50 mg/mL (69.67 mM) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Cell experiment: 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 experiment: 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.

Background

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

Pan-RAS-IN-1 binds to KRasG12D-GppNHp with an affinity less than 20 μ M. 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 μ M treatment[1].

Pan-RAS-IN-1 administration results in inhibition of tumor growth over 15 days of treatment. Pan-

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

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].

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

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA