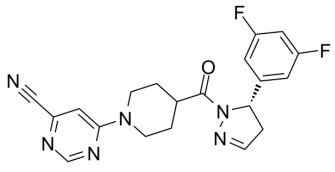
GSK547

Cat. No.:	HY-114492
CAS No.:	2226735-55-1
Molecular Formula:	$C_{20}H_{18}F_2N_6O$
Molecular Weight:	396.39
Target:	RIP kinase
Pathway:	Apoptosis
Storage:	-20°C, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (630.69 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5228 mL	12.6138 mL	25.2277 mL
5 mM	0.5046 mL	2.5228 mL	5.0455 mL
10 mM	0.2523 mL	1.2614 mL	2.5228 mL

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

In Vivo

1. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.31 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (5.25 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (5.25 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.25 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GSK547 (GSK'547) is a highly selective and potent inhibitor of receptor-interacting serine/threonine protein kinase 1 (RIPK1), inhibits macrophage-mediated adaptive immune tolerance in pancreatic cancer[1].

IC_{50} & Target

RIP1[1]

In Vitro

GSK547 (0.1-100000 nM; 24 hours) pretreats L929 cells with recombinant TNFα and zVAD at various doses for 30 min, then cell death is induced with an IC_{50} of 32 nM after 24 hours[1].

GSK547 up-regulates STAT1 signaling in bone marrow-derived macrophages (BMDM)[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	L929 cells (Mouse L-cells NCTC 929)
Concentration:	0.1 nM; 10 nM; 1000 nM; 100000 nM
Incubation Time:	24 hours
Result:	Reduced viability of L929 cells after co-treatment with TNFα and zVAD with an IC_{50} of 32 nM.

Western Blot Analysis[1]

Cell Line:	Bone marrow-derived macrophages (BMDM)
Concentration:	
Incubation Time:	30 minutes
Result:	Up-regulated STAT1 signaling in BMDM.

In Vivo

GSK547 (GSK′547; RIP1i) robustly targets RIP1 in vivo. RIP1 inhibition results in immunogenic macrophage differentiation in pancreatic cancer, leading to adaptive immune activation and tumor protection for pancreatic ductal adenocarcinoma (PDA)[1].

GSK547 (100 mg/kg/day; fed via food-based dosing; 15-50 days) reduces tumor burden and extends survival compared with mice treated with controls or Nec-1s[1].

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Animal Model:	The wild-type (WT) mice orthotopically implanted with $Pdx1^{Cre}$;$Kras^{G12D}$;$Trp53^{R172H}$ (KPC)-derived tumor cells[1]
Dosage:	~100 mg/kg
Administration:	Fed via food-based dosing, daily, 15-50 days
Result:	Reduced tumor burden and extended survival.

REFERENCES

[1]. Wang W, et al. RIP1 Kinase Drives Macrophage-Mediated Adaptive Immune Tolerance in Pancreatic Cancer. Cancer Cell. 2018 Nov 12;34(5):757-774.e7.

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

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