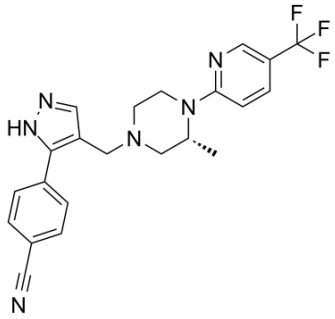
GNF362

Cat. No.:	HY-126750
CAS No.:	1003019-41-7
Molecular Formula:	$C_{22}H_{21}F_3N_6$
Molecular Weight:	426.44
Target:	Phosphatase
Pathway:	Metabolic Enzyme/Protease
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 : 125 mg/mL (**293.12 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3450 mL	11.7250 mL	23.4500 mL
	5 mM	0.4690 mL	2.3450 mL	4.6900 mL
	10 mM	0.2345 mL	1.1725 mL	2.3450 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: ≥ 2.08 mg/mL (4.88 mM); Clear solution
2. Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
   Solubility: ≥ 2.08 mg/mL (4.88 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

GNF362 is a selective, potent, and orally bioavailable inhibitor of **inositol trisphosphate 3′ kinase B (Itpkb)** with an **IC $_{50}$** of 9 nM. GNF362 also inhibits Itpka and Itpkc with **IC_{50}** values of 20 nM and 19 nM, respectively. Inositol trisphosphate 3′ kinase B (Itpkb) is a Ca^{2+}-dependent kinase, which phosphorylates the 3′ position of Ins (1,4,5) P3 to generate inositol 1,3,4,5-tetrakisphosphate [Ins (1,3,4,5) P4][1].

In Vitro

GNF362 (0-10 mM) blocks Ins (1,3,4,5) P4 production, enhances antigen receptor-driven Ca^{2+} responses and lead to apoptosis of activated T cells in an Itpkb-dependent manner in lymphocytes[1].
GNF362 augments SOC responses following antigen receptor cross-linking, with an EC_{50} of 12 nM in primary B or T lymphocytes[1].

In Vivo

GNF362 (orally administration; 6 or 20 mg/kg; twice daily; 21 days) shows minimal block in antibody production but shows significant inhibition of joint swelling at 6 mg/kg, reduces inflammatory cell infiltrate, joint damage, and proteoglycan loss at 20 mg/kg[1].

Animal Model:	A Lewis rat antigen-induced arthritis (rAIA) model[1]
Dosage:	6 or 20 mg/kg
Administration:	Orally administration; 6 or 20 mg/kg; twice daily; 21 days
Result:	Reduced knee swelling in both the 20mg/kg and 6mg/kg treatment groups of GNF362 by 47% and 34%, respectively.

REFERENCES

[1]. Miller AT, et al. Conversion of antigen-specific effector/memory T cells into Foxp3-expressing Treg cells by inhibition of CDK8/19. Sci Immunol. 2019 Oct 25;4(40). pii: eaaw2707.

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