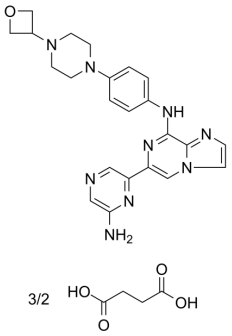
Lanraplenib succinate

Cat. No.:	HY-109091B
CAS No.:	1800047-00-0
Molecular Formula:	$C_{23}H_{25}N_9O.{}_3/_2C_4H_6O_4$
Molecular Weight:	620.64
Target:	Syk
Pathway:	Protein Tyrosine Kinase/RTK
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 83.33 mg/mL (134.26 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6112 mL	8.0562 mL	16.1124 mL
	5 mM	0.3222 mL	1.6112 mL	3.2225 mL
	10 mM	0.1611 mL	0.8056 mL	1.6112 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 (3.35 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.35 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Lanraplenib succinate (GS-9876 succinate) is a highly selective and orally active SYK inhibitor (IC_{50}=9.5 nM) in development for the treatment of inflammatory diseases. Lanraplenib succinate (GS-9876 succinate) inhibits SYK activity in platelets via the glycoprotein VI (GPVI) receptor without prolonging bleeding time (BT) in monkeys or humans[1][2][3].

IC_{50} & Target

IC50: 9.5 nM (SYK)[1]

In Vitro

Lanraplenib succinate (GS-9876 succinate) inhibits anti-IgM stimulated phosphorylation of AKT, BLNK, BTK, ERK, MEK, and PKCδ in human B cells with EC_{50} values of 24-51 nM. Lanraplenib monosuccinate inhibits anti-IgM mediated CD69 and CD86 expression on B-cells (EC_{50}=112±10 nM and 164±15 nM, respectively) and anti-IgM /anti-CD40 co-stimulated B cell proliferation (EC_{50}=108±55 nM). In human macrophages, Lanraplenib succinate inhibits IC-stimulated TNFα and IL-1β release (EC_{50}=121±77 nM and 9±17 nM, respectively)[1].

Lanraplenib succinate (GS-9876 succinate) inhibits glycoprotein VI (GPVI)-induced phosphorylation of linker for activation of T cells and phospholipase Cγ2, platelet activation and aggregation in human whole blood, and platelet binding to collagen under arterial flow[2].

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

REFERENCES

[1]. Di Paolo J, et al. FRI0049 Preclinical Characterization of GS-9876, A Novel, Oral SYK Inhibitor That Shows Efficacy in Multiple Established Rat Models of Collagen-Induced Arthritis.Annals of the Rheumatic Diseases 2016;75:443-444.

[2]. Clarke AS, et al. Effects of GS-9876, a novel spleen tyrosine kinase inhibitor, on platelet function and systemic hemostasis. Thromb Res. 2018 Oct;170:109-118.

[3]. Kivitz AJ, et al. GS-9876, a Novel, Highly Selective, SYK Inhibitor in Patients with Active Rheumatoid Arthritis: Safety, Tolerability and Efficacy Results of a Phase 2 Study [abstract]. Arthritis Rheumatol.2018; 70 (suppl 10).

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