Lanraplenib monosuccinate

Cat. No.: HY-109091A

CAS No.: 1800046-97-2

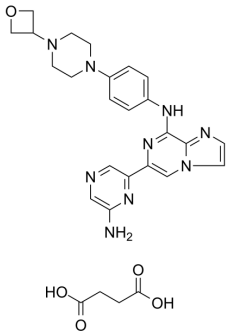
Molecular Formula: $C_{27}H_{31}N_9O_5$

Molecular Weight: 561.59

Target: Syk

Pathway: Protein Tyrosine Kinase/RTK

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (222.58 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7807 mL	8.9033 mL	17.8066 mL
	5 mM	0.3561 mL	1.7807 mL	3.5613 mL
	10 mM	0.1781 mL	0.8903 mL	1.7807 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 (3.70 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.70 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Lanraplenib monosuccinate (GS-9876 monosuccinate) is a highly selective and orally active SYK inhibitor (IC_{50}=9.5 nM) in development for the treatment of inflammatory diseases. Lanraplenib monosuccinate (GS-9876 monosuccinate) 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 monosuccinate (GS-9876 monosuccinate) 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 monosuccinate inhibits IC-stimulated TNFα and IL-1β

release (EC_{50}=121±77 nM and 9±17 nM, respectively)[1].

Lanraplenib monosuccinate (GS-9876 monosuccinate) 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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